

Innovation: what's in a word?

There is a certain familiarity to British observers in the set of proposals announced last week to stimulate technological innovation in US industry. "Generic technology centers", based at universities and partly supported by industry, have been an active element of Science Research Council policy for several years. Close university/industry links are already enshrined in the SRC's teaching companies scheme and the now flourishing cooperative awards for science and engineering (CASE) fellowship programme. The National Research Development Corporation will be pleased to learn that the US proposal to establish a network of state and regional corporations for innovation development are partly based on its "successful", example — and there will even be annual "President's awards to industry" similar to those bestowed by the Queen on British industry for over a decade.

In Britain, these various developments have taken place in a piecemeal fashion over a number of years, a gradual process of moulding government intervention in the process of technological development, with increasingly important implications for research policy. In the US, they have been put together into a single package which President Carter referred to as a "first step" in supporting industrial innovation as a spur to international competitiveness and domestic entrepreneurship. And also included in the package are a complex set of legislative and administrative proposals ranging from anti-trust rules to technical information services.

The advantage of such packaging is that it provides a central theme around which otherwise disparate activities can be arranged — and Dr Frank Press, the President's Science Adviser, who initially proposed the studies leading to last week's proposals, points out that one immediate effect has been a heightened awareness of the concept of innovation within the administration. The problem, however, is that innovation itself is a slippery concept that is almost impossible to define. And any claim that it is going down (or even up) can only be made on indirect evidence, such as measurements of productivity, or the level of research and development budgets.

Successful innovation, like invention or creativity, cannot be legislated for. The best that can be done is to identify what are considered to be the key variables, and manipulate them in what is considered an effective way. This is partly a matter of technological and economic analysis. But it can also mean the insertion of political or value judgements necessary to short-cut the analysis and make policy decisions possible.

The danger here is that in the absence of hard data, powerful mythologies may be introduced — and subsequently planned for — to legitimate broad-based policy initiatives. In the UK, one such mythology has been to blame a recalcitrant labour force as the major force obstructing innovation, when in practice the problem is part of a complex of domestic and international processes. Poor labour-management relations may well be a part,

but other factors, such as international competition and skyrocketing energy costs, are just as much to blame.

In the US, there is another myth, that of a lost Yankee ingenuity, the Holy Grail often quoted as the main cause of economic strength and technological superiority, now dimmed by a rising tide of regulation. The problem is that a number of sectors of US industry can be identified — electronics, pharmaceuticals, and biotechnology in general might be quoted as typical examples — where innovation (and profitability) are very far from dead. And again there are external factors, in particular the growing strength of Japan and Germany as technological powers, which may give the appearance of US decline, but can provide only relative rather than absolute measurements.

Certainly the US economy is not as strong as it might be. And declining productivity is an important contributor to double-digit inflation. But there are dangers in reducing the problem to a purely technical one, in particular since this may divert attention from other, equally important, aspects of technological change.

Three of these aspects may be mentioned. The first is the impact of technology on the natural and social environment. Regulation needs to be placed on a rational basis if it is effectively to achieve its intended purpose. In practice, levels of regulation are increasingly being set as the balance of economic against social goals, with the emphasis being shifted back to the former — and this form of rationality speaks less of enlightenment philosophy than of political pragmatism.

The second aspect is the impact of technology policy on developing countries. The United Nations Conference on Science and Technology for Development, held earlier this year in Vienna, drew attention to the ways in which the conditions set by the developed countries for the exploitation of knowledge — for example, on patent and licence policies — can affect the Third World's development prospects. Yet there was virtually no consideration of this particular problem within the US innovation review and the subsequent presidential proposals.

Finally, there are the effects of technological change on the labour force. President Carter, stating that labour's main interest is in early warning about changes, is planning a new labour/technology forecasting system to predict the consequences. But there are many predictions that some aspects of innovation — and in particular the structural unemployment that may well result from the increasing automation of production — will be severe, and that more than advance warning may be necessary.

The Kemeny Commission on the accident at Three Mile Island has warned of the danger of concentrating so hard on the adequate performance of mechanical systems that one fails to pay sufficient attention to the gaps and shortcomings in the social systems which support them. It would be a pity if the current concern with technological innovation were to lead policy-makers further in the same direction. □



End nuclear complacency — 3 Mile Island Report

"The US Nuclear Regulatory Commission is currently unable to produce an acceptable level of safety for nuclear power" says John Kemeny, Chairman of the President's Commission on the 3 Mile Island Disaster. **David Dickson** reports on the Commission's findings that human failures led to the escalation of what might have been a minor incident into a major disaster



President Carter visits the TMI control room. At the height of the collapse 100 alarms were ringing

THE public inquiry into last March's accident at the Three Mile Island nuclear plant has resulted in a damning indictment of official attitudes towards the safety of nuclear power.

In its final report, presented to President Carter last week, the 12-member commission which carried out the inquiry strongly criticises the nuclear industry for underplaying the risks associated with the operation of nuclear power plants — and the Nuclear Regulatory Commission for failing to apply adequate controls.

The industry has taken comfort from the commission's final decision — agreed despite a number of closely contested votes — not to recommend a moratorium on the construction of new plants until some of the inadequacies which the report identifies have been put right.

But it has not seriously questioned the commission's major finding: that "fundamental changes" are necessary in the organisation, procedures and practices of both the industry and the NRC if similar accidents are to be prevented in the future, and the risks of nuclear power are to be kept within "tolerable limits".

The commission's report is particularly critical of what it calls the "mindset", widely propagated by industry, that nuclear power plants are basically safe. "The Commission is convinced that this attitude must be changed to one that says nuclear power is, by its very nature, potentially dangerous", it states.

The report also points out that the operating company, Metropolitan Edison, failed to change any instructions to its operators following a similar accident which had occurred at another plant in September 1977, despite strong recommendations for making this change by a senior engineer from Babcock and Wilcox.

The report demands wide-reaching changes in the training of both plant operators and managers, expressing concern at the relative neglect of human factors in nuclear safety. The commission

says this neglect is itself a product of a "mindset" preoccupied with the safety of equipment, rather than the ability of operators and management to respond to an emergency.

Other recommendations passed to President Carter include proposals that future reactors should be located "in areas remote from concentrations of population", rather than merely using the concept of "low population zones"; that the NRC be reorganised, with a single director replacing the current five commissioners; that an oversight committee on reactor safety be established of up to 15 people from a range of backgrounds to monitor all aspects of the risks of nuclear power; and that a utility applying for an operating licence must show that the state in which its nuclear plant is to be situated has an officially-approved emergency response plan.

How it happened

The report provides a graphic description, based on evidence received over several weeks of public hearings, of how the events unfolded that led to the worst accident in the history of the US nuclear programme. And the description also reveals how human action — and inaction — transformed a series of minor technical failures into a disaster.

According to the commission, the triggering event was a "fairly routine malfunction" in the equipment which purifies the water condensate from the steam turbine inside the plant. The turbine automatically stopped, soon followed by the automatic shut-down of the reactor.

To prevent the water pressure inside the reactor vessel from increasing, a pilot-operated relief valve opened automatically; however when the pressure dropped again, the valve failed to close — allowing the coolant water to escape.

Events built up rapidly from there. Confusion over indicator lights led the operators to believe that the valve had closed. A high-pressure injection system

came on automatically; but the operators thought this was filling the plant too quickly with water, and cut the flow from 1000 to 100 gallons a minute. The net result of the sequence of events that followed was that the reactor core gradually became uncovered — leading to eventual fears of a core melt-down.

The human failures attract the particular attention of the Kemeny Commission, since without these, it suggests, the accident would have been far less significant. The specific problem was a failure to recognise the actual conditions of the plant; but it relates these to much wider problems of competence, background and training of both operators and management.

"As the evidence accumulated, it became clear that the fundamental problems are people-related problems not equipment problems", the report states. "We do not mean to limit this term to shortcomings of individual human beings — although those do exist. We mean more generally that our investigation has revealed problems with the 'system' that manufacturers, operates and regulates nuclear power plants."

Some of these failures are listed in detail in an analysis prepared by commission staff on the selection, training, qualification and licensing of operating personnel. This report points out, for example, that there is no minimum eligibility requirements for operators laid down by the NRC for factors such as education, experience, reliability, or psychological fitness.

Although operator examinations were consistent with regulations, it says, they did not ensure that candidates for a licence had an in-depth knowledge of nuclear reactor theory, design and operation. Training for operators concentrated on systems, equipment and procedures rather than basic scientific and technological concepts, such as thermodynamics, enthalpy, decay heat production, or solid system operation.

(A spokesman for General Public Utilities Corporation responsible for

running the plant defended their operators' competence by pointing out that over the period 1975 to 1978, TMI control room operators ranked ninth out of 30 facilities in NRC examination performance; commission members say that this merely indicates the size of the problem.)

Another failure is shown up by the short sentence "utility management did not require attention to detail as a way of life at Three Mile Island." The report goes on to list 23 instances, ranging from relatively minor deficiencies in control room practices to major short-comings in failing to correct faulty equipment, or to identify a group with special responsibility for acting on safety concerns raised by employees.

It also raises major questions about the quality control of important components. For example the report points out that although the operating company, Metropolitan Edison, has a quality assurance programme meeting NRC requirements, these did not apply to the plant as a whole, but only to systems classified as 'safety-related'.

The valve which stuck open, was not classified as 'safety-related'. "In addition, the NRC did not require the level of independent review normally found in the quality assurance programmes of safety-critical industries", the report says. Nor did Met Ed go beyond NRC requirements in applying quality controls to equipment such as radiation monitors or control rod drive mechanisms.

It was therefore a combination of poorly prepared operators and management, plus a lack of attention to relatively minor safety details, that made an accident such as that at Three Mile Island "eventually inevitable" says the report. "Large-break accidents require extremely fast reaction, which therefore must be automatically performed by the equipment. Lesser accidents may develop much more slowly and their control may be dependent on the appropriate reactions of human beings", it says.

Basic flaw

Scientists and engineers had worried for decades about the safety of nuclear equipment, but their approach to nuclear safety had a "basic flaw", namely a pre-occupation with large-break accidents, and the attitude that if they could be controlled, it was not necessary to worry about the analysis of "less important" accidents.

"This was the tragedy of Three Mile Island, where the equipment failures were significantly less dramatic than those that had been thoroughly analysed, but where the results confused those who managed the accident."

Another problem, says the report, was that information about conditions inside the plant was not presented in the control room in a clear and understandable form. At one point, soon after the valve had stuck open, there were over 100 alarms ringing in the control room, with no system for indicating which way was most important.

Among the other findings of the commission were:

●Health effects: The commission says that the most serious health effect of the accident was severe mental stress, this being highest among those living within 5 miles of the plant, and in families with preschool children.

Since most of the radiation was contained within the plant — it calculates less than 0.01% of the radioactive iodine released from the fuel escaped into the environment, and that no detectable amounts of caesium and strontium escaped — the health effects of the accident would be minimal. The commission says it can be "practically certain" that there will be less than 10 extra cancer deaths in the 325,000 people living within a 50-mile radius, and that it is highly likely there will be no extra deaths.

●Costs: The commission estimates that, discounting health costs, the cost of the accident will be between \$1 billion and \$2 billion, much of this being the cost of replacement power. If the plant can not be put back into operation, the cost will be much higher, it says.

●Seriousness of accident: Examination of several different scenarios that could have taken place included some which would have resulted in a "melt-down". Under this scenario, the fuel would reach such a temperature that it would melt through the steel reactor vessel and reach the floor of the containment building, where its heat would be dissipated by water.

The commission calculated that even if a melt-down occurred, there was a high probability that the containment building and the hard rock on which it is built would have been able to prevent the escape of a large amount of radioactivity. But it points out that, since the calculations are at the limits of engineering knowledge, they include a degree of uncertainty.

●Public and worker health and safety: The commission says that there is inadequate knowledge of the effects of low levels of ionising radiation, of strategies to mitigate the health hazards of exposure to radiation, and of other areas relating to regulation setting to protect health and public health.

It points out that state organisation in Pennsylvania did not have adequate resources for dealing with radiation health programmes relating to the operation of Three Mile Island. And that the utility was not required to, and did not, keep a record on workers of the total work-related plus non-work related radiation exposure.

It recommends more emphasis on research on the health effects of radiation co-ordinated under the National Institutes of Health, as well as an increased programme for educating health professional and emergency response personnel in the vicinity of nuclear power plants.

●Nuclear Regulatory Commission: The report spells out in detail criticisms of the

shortcomings of the NRC in dealing with the accident, in particular its apparent indecisiveness, and uncertainties in diagnosing the situation inside the plant. It points out, for example, that NRC officials wrongly concluded on the second day that there was a danger that a hydrogen bubble in the reactor vessel might explode through contact with oxygen produced through water radiolysis, which other scientists later pointed out was impossible.

One of the main conclusions of the commission is that the NRC should be restructured. "The totality of our findings is that no-one is running that particular agency."

'Bark worse than bite'

Reaction to the Kemeny Commission's report has been predictably diverse. Nuclear critics argue that the report does not go far enough in following through the logic of its own conclusions, and that the report's bark may therefore turn out worse than its bite.

"We are still left with the problem of the 70 plants that are already operating in this country, many of which should be temporarily shut down until adequate safety can be guaranteed. We need a whole new approach to the safety of our nuclear programme which goes far beyond administrative juggling", says Professor Henry Kendall, professor of physics at the Massachusetts Institute of Technology, and a co-founder of the Union of Concerned Scientists which has been criticising federal safety measures for several years.

The nuclear industry, carefully side-stepping some of the stronger criticism in the report, has interpreted its message as "proceed with caution" — and points out that it has already been doing much to improve safety procedures following the accident.

"It is evident that the commission found nothing in the wake of TMI that suggests that nuclear power plants as presently designed and built are unsafe," says Darl Walske, president of the industry-sponsored Atomic Industry Forum.

But conventional attitudes — the "mindset" referred to by the Kemeny Commission — retain a strong grip. Three weeks ago the *Washington Post* carried a two page advertisement in which Dr Edward Teller claimed "I was the only victim of Three-Mile Island", since he suffered a heart attack resulting from strenuous efforts to answer anti-nuclear critics; the main lesson of the accident, he said, was that "nuclear reactors are even safer than we thought".

Last week NRC commissioner Peter Bradford wrote to the newspaper accusing Dr Teller of misleading the public — and pointing out that the advertisement had been paid for by the firm which produced the valve which had stuck open at Three Mile Island. □

US boosts university-industry links

After 18 months' study by the Commerce Department, President Carter last week made 32 proposals for increasing the commercial exploitation of scientific knowledge. **David Dickson reports.**

PRESIDENT Carter is demanding that federal agencies substantially increase their efforts to stimulate links between the university research community and private industry. Building on the recent experience of the National Science Foundation, he has recommended that the government raise its support for such efforts by \$150 million a year.

The recommendation is one of 32 which the President made last week in a message to Congress on new initiatives to stimulate industrial innovation.

Describing the package of recommendations, the fruits of an 18-month study by the Commerce Department, as a "first step" towards meeting the nation's commitment to innovation, he said they would help "the continuing challenge to maintain the economic strength of the US economy."

The review was initially recommended by Dr Frank Press, director of the Office of Science and Technology Policy. Its basic premise was that many of the nation's economic problems can be related to a decline in the rate of productivity; and that this in turn has been partly caused by a decline in innovation, as implied by factors such as declining investment in research and development and a decrease in the number

of patent applications.

Many of the President's recommendations directly involve research. Yet rather than concentrate on ways of increasing direct federal support for research of interest to industry, the President's recommendations focus instead on the environment in which both research and innovation take place — and thus how the government can alter this environment to make it more conducive to economic growth.

The review therefore covered all aspects of the innovation process, from anti-trust policy to technical information systems, making numerous proposals for legislative and administrative changes. In the short-term, however, a principal beneficiary of the review is likely to be the National Science Foundation, budgeted to receive about \$30 million of the extra \$55 million which the President suggested needs to be spent in 1981.

The purpose of the NSF money will not primarily be to support further research — although this will obviously be one effect — but to open up the arteries connecting universities to private corporations. In this way it is intended to help to lead to what Secretary of Commerce Mrs Juanita Kreps referred to as "a more effective partnership

among government, industry, labour, and the academic community."

In particular, the NSF's budget request for 1981 will include a three-fold increase in support of a programme introduced last year to finance research proposals jointly submitted by university and industry research workers. NSF officials point out that the programme, scheduled to increase from \$8 million to almost \$30 million, has already attracted the involvement of major corporations such as Westinghouse, Union Carbide and Monsanto.

President Carter has now suggested that the NSF experience be used as a test-bed for cooperative projects sponsored by other federal agencies, such as the Department of Defense, the Department of Energy and the Environmental Protection Agency, and that an aggregate target of \$150m be eventually aimed for.

Furthermore in view of the historical importance which small entrepreneurial firms have played in bringing new products to the market-place, he is proposing to increase the budget of the NSF's Small Business Innovation Research Programme from \$2.5 million to \$10 million. Again this would be used as the basis of a \$150 cross-agency effort.

"The innovation review makes clear

The new innovation initiatives in detail

SOME of the main initiatives announced by President Carter to spur industrial innovation in last week's message to congress:

- Four "generic technology" centres will be established at universities and other private sector sites to encourage research and development in fields such as corrosion prevention, automated assembly, and tribology. Each centre will be jointly financed by industry and government, with the latter's share dropping to 20% or less by the fifth year. Three centres will be established in 1981 by the Department of Commerce, and one by the National Science Foundation, at a cost of about \$6 to \$8 million.

- The NSF will receive an additional \$20 million in 1981 to increase its efforts at linking industry with university scientists. The foundation will also work with other agencies to initiate similar cooperative R&D programmes, with an eventual aggregate target of \$150 million.

- The federal government will seek legislation to establish a uniform patent policy. Under this legislation, title to a patent resulting from federally-funded research would be retained by the government, but contractors would obtain exclusive licenses in specified

fields of use. Small businesses and universities, however, would be allowed to retain patent ownership "in recognition of their special place in our society"

- The Department of Justice will clarify the role of anti-trust legislation with respect to research collaboration between different companies

- The NSF's Small Business Innovation Research programme will be expanded from \$2.5 million to \$10 million in 1981. The foundation will help other agencies develop similar programmes, under the co-ordination of the Office of Management and Budget, with an aggregate target of \$50 million

- Increased assistance will be provided to establish Corporations for Innovation Development (CIDs) on a state or regional basis, to help entrepreneurs gain access to investment capital

- To help minimise the impact of regulation, executive health, safety and environmental regulatory agencies will prepare five-year forecasts of their priorities and concerns. "Better knowledge of agency plans will allow industry to plan its research and development" says the administration

- In addition, federal executive agencies responsible for reviewing the safety and efficacy of products will develop and

implement a system of priorities. Under these systems, the agencies will identify those products that are most innovative and/or have exceptional social benefits, and expedite their clearance reviews "to the extent permitted by applicable statutes"

- The Secretary of Labour and the Secretary of Commerce will work with labour and management to develop a national Labour/Technology Forecasting System. This system would develop advance warning of industrial changes and permit timely adjustments

- The Commerce Department and the NSF will host a national conference for deans of business and engineering schools to stimulate improved curriculum development in technology management and entrepreneurship

- The National Technical Information Service will establish a new center, at an annual budget of up to \$2 million, whose purpose will be to improve the flow of knowledge from federal laboratories and R&D centres to private industry

- The President will establish an annual award for technological innovation in the six areas of transportation, communication, health, agriculture and food, and natural resources (including energy). The awards will be presented by the President's science and technology adviser. □

how extensively innovation depends on R & D, especially on long-term research. But the expertise in universities has not been used as extensively as possible to support industrial innovation. The NSF programme has already shown successes, and it is time to expand this effort," says Dr Press.

Congressional response to the package, promised since last April, has been lukewarm. Some proposals, such as the setting up of "generic technology centres" and the introduction of uniform patent policy, have been generally welcomed; indeed many are already part of legislative

proposals currently before Congress.

At a Senate hearing last week, however, several Congressmen criticised the package for not including any tax incentives related to R & D expenditures. Administration officials replied that these would come later, as part of a complete set of tax reforms; and Dr Jordan Baruch of the Commerce Department said that tax incentives might not be a sharp enough instrument to attack such a complex issue.

Senator Adlai Stevenson criticised the package for lacking imagination. "It is a first step, but I am not convinced that the Executive Branch has got the guts to take

the next ones needed to reach a rational technology policy" he said. Mr Stevenson quoted in particular Japan's recently announced plans to stimulate government support across a wide range of technological areas, from ocean mining to integrated circuits.

"For 25 years the question of innovation has been around," replied Dr Press. "For the first time the President has come forward with definite proposals; I think this is an important step. And US industrial leaders that I have spoken to would not want to touch what the Japanese are doing with a ten-foot pole." □

Soviets announce build-up to fusion power

RECENT Soviet developments in energy were conspicuous by their absence from the agenda of last week's UK-Soviet energy symposium in Moscow. To some extent, this was to be expected, since the prime aim of the symposium was to explore areas of possible cooperation in the near future. Nevertheless, even in his exposition of the long-term "second stage" of the new Soviet energy "strategy", the Minister of Power and Electrification, Peter S. Neporozhnyy, made no allusion at all to the Soviet Union's latest step in power generation — the start-up of the first module of the Angara-5 fusion generator.

This is all the more remarkable since the demonstration run of the Angara-5 module, early in October, was given considerable media coverage for both home and foreign consumption. The Angara-5 is an electron beam device, the name, according to *Pravda*, signifying the five tributaries (the beams) which flow into lake Baikal (the tritium/deuterium target), and issue thence as the mighty Angara river (the energy produced). Last month's test of the module was carried out at the Kurchatov Atomic Energy Institute; according to Valerii Legasov, the Deputy Director, after "through experiments" have been carried out with each of the 48 modules, a "demonstration" Angara-5 will be built at the institute's test site.

No indication, has so far been given of when the break even point may be expected, although Moscow radio's "World Service" suggested that the first power plants based on Angara-5 will be built by the end of the century. At all events, practical use of the Angara-5 lies too far in the future to merit a place in Neporozhnyy's "strategy", although his outline of the "second stage" did include some references to MHD and fusion generation.

In MHD, he said, work would go forward on improving conversion efficiency and hinted that "energy and magnetic field parameters close to commercial" were already within reach on one experimental device. Fusion research, he said, would continue using both Tokamak and laser techniques. Already plasma temperatures only 4-5 times less

than those required for sustained reaction, he said, had been attained.

The majority of the symposium, however, was devoted to the first stage of the strategy; development of the coal industry, including low grade coals to be used in generating stations close to the mines, expansion of the Siberian hydroelectric network and the phasing out of oil and gas-fired power stations.

Although the Soviet planners still claim ample reserves of oil and gas, they are now ready to admit that these lie in increasingly remote and extreme terrains, and that exploitation costs will become increasingly expensive. Indeed, for the first time, they are prepared to admit small and temporary shortfalls in production. In the not too far future, the Soviet participants in the symposium agreed, oil will have to be reserved for oil-specific industries — transport and petrochemicals.

Nuclear generation will to a large extent replace oil in the power sector. Although the extension of the Union-wide "supergrid" of 1500 V DC transmission lines should, theoretically, allow power

stations to be sited anywhere, the old paradox of the Soviet energy map (80% of resources east of the Urals, 80% of consumption west of the Urals) is being perpetuated in the siting of future nuclear power stations, close to the consumers.

Hardly a mention, even in informal discussions, was made during the symposium of Academician Sollezhnitsky's recent proposals for nuclear generating "complexes" in Siberia. The safety and ecological aspects raised by Dollezhal' were barely alluded to, and the plans for nuclear "boiler houses" for district heating in major cities were given great prominence; with, perhaps, one small difference.

Until now, Soviet commentators have suggested that the nuclear boiler houses would be situated in the suburbs of the cities, with a "safety-zone" of some 1-2 km around them, reserved for industrial and leisure use (but not housing). Now, however, according to Neporozhnyy, the boiler houses may be further away — transmission of the hot water for up to 50 km, he said, is reckoned to be "economic". Vera Rich

Hungarian reactor to be made 'safe'

CONSTRUCTION of the Paks nuclear power station, which should supply one third of Hungary's present peak power demand, is at last on schedule. Last year, the station, whose construction had been running late since 1975, was the subject of special resolutions by the Council of Ministers and the Party Politburo. A new management system was set up, with government commissioners working on the site. Shortly afterwards, building operations were reported to have "speeded up considerably", although the workforce of 5200 is still insufficient and more managerial changes are envisaged if the original schedule is to be maintained.

This acceleration, however, has not been achieved at the cost of safety. Out of the 60,000 million forints (£1,500 million) which the station will cost, 12,000 million (20%) will be spent on safety measures.

The Hungarian planners are in a somewhat delicate position as regards

safety. The country is small, with no convenient expanse of empty land in which to site a reactor. Moreover, Austrian TV reaches considerable areas of Hungary, and although any evidence on the subject can only be anecdotal, there is good reason to believe that the population at large was considerably perturbed by the "anti-nuclear" verdict of the Austrian referendum earlier this year.

Perhaps for this reason, a recent Budapest TV programme describing the Paks station paid especial attention to its safety precautions. "Triple walls", said the commentator, separate radioactive materials from the environment. The outermost of these walls, from his description, is simply a steel and concrete containment vessel — of the type, until recently, dismissed by Soviet planners (who are intimately involved in any Comecon nuclear power station) as a Western capitalist ploy to inflate costs. □

EPA panel recommends postponement of 2, 4, 5-T hearings

THE herbicide 2, 4, 5-T poses no "substantial hazard to human health or to the environment" according to a report prepared by the Scientific Advisory Panel of the section of the US Environmental Protection Agency concerned with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Accordingly, the panel recommends that the final hearings to consider the validity of the ban on 2, 4, 5-T be postponed until more information on the carcinogenicity and reproductive toxicity of the herbicide and its 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (dioxin) contaminant is available.

The EPA enforced a ban on the use of 2, 4, 5-T in March of this year following a study in the state of Oregon which linked an increase of spontaneous abortions in the area to spraying with the herbicide (*Nature* 8 March, page 108). The initial ban was restricted to use of the herbicide in forestry but since then has been made total and applies to all applications of 2, 4, 5-T.

Law Court and EPA hearings have been held at intervals since March to consider the merits of the ban. The final hearings,

initially scheduled for October 1979 have been postponed until January 1980 and if the advisory panel has its way will be postponed even longer.

The panel's report is based on evidence presented by interested parties at two open meetings held during the summer. Following the meetings, the panel agrees that the EPA is correct in stating that 2, 4, 5-T and dioxin are teratogens and fetotoxins. It also takes the EPA view that as dioxin is carcinogenic in test animals it may be a "potential human carcinogen."

But the panel disagrees with the EPA's opinion that human exposure "from spray drift and the water environment is likely to be broad or substantial" where 2, 4, 5-T use on rice is concerned. As for the use of the herbicide on rangeland the panel says there is no "convincing argument of an immediate or substantial hazard" to humans.

Dow Chemical Company is the major producer of 2, 4, 5-T in the US and stands at the forefront of the campaign to have the ban on 2, 4, 5-T lifted. The company insists that there is no good scientific evidence to

support the ban. Dow scientists admit that dioxin is extremely toxic but state that it is not present in sufficient concentrations to pose a human health hazard.

The Advisory Panel points out that on some questions the EPA position is "relatively close to that of the scientists from the Dow Chemical Company". In contrast to the view put forward by the EPA that there is no safe level for dioxin in rats and mice the panel says that such a statement is incorrect. And it suggests that a review of the evidence shows that the EPA and Dow Chemical are not as far apart on this issue as it might seem.

It remains to be seen whether this internal vetting process will have any influence on the EPA's actions on 2, 4, 5-T. The results of the report will give a considerable boost to Dow's campaign and the company for public relations reasons, may well agree with the final recommendations of the panel, that in view of the potential toxicity of dioxin "efforts should be made to further reduce" its level in commercial preparations of 2, 4, 5-T.

Alastair Hay

Pathogens panel should have lay representation, says UK health minister

THE new Conservative government, like its predecessor, is taking into account the recommendations of the Shooter Report on the outbreak of smallpox in Birmingham last year in drawing up new regulations for the safe handling of dangerous pathogens during research work and diagnosis. Mr Patrick Jenkin, Secretary of State for Health, told a meeting organised by the Association of Scientific, Technical and Managerial Staffs (ASTMS) in London last week, that the government is planning to implement many of the Shooter recommendations and also some of those made by the Health and Safety Executive in its recent publication 'Dangerous Pathogens: draft regulations and draft guidance notes'.

Under the government's new proposals, notification of intention to work with category A pathogens (the most dangerous) would be compulsory, said Mr Jenkin, and laboratories would have to be inspected by HSE inspectors before work could begin. They would then have to be inspected regularly against a checklist which is to be drawn up in accordance with recommendations laid down by Shooter. Laboratories researching with category A pathogens would also have to be sited outside densely populated areas.

The government has set up a panel which is currently looking into the workings of the Dangerous Pathogens Advisory Group (DPAG), a committee of experts currently under the auspices of the Department of Health and Social Security (DHSS) which

was set up in 1973 to administer a system of voluntary control of work with category A pathogens. According to Mr Jenkin, the panel is likely to recommend that a new body be set up with an expert and lay membership, including professional, trade union and public interest representatives. This body should remain under the aegis of the DHSS and would administer the new compulsory system of notification.

The position with public health laboratories is different because they are mainly concerned with category B pathogens which do not have to be notified to DPAG. There could come a time, however, said Mr Jenkin, when notification for category B pathogens would also become compulsory. Nevertheless, he assured the meeting that it is still the government's intention to implement within three years the recommendations for improved safety in public health service laboratories laid out in the Howie report published last year. "It would inevitably cost the National Health Service a lot of money to bring all its labs up to the standard of the Howie report", he said, but the government thought that the £7 million (1978 prices) needed could be found.

Clive Jenkins, General Secretary of ASTMS, agreed with the opening up of membership of DPAG to non-experts. "Free standing committees of experts are things of the past", he said and added that a body along the same lines as the Genetic Manipulation Advisory Group (GMAG)



Patrick Jenkin: reforming DPAG

would be appropriate: "GMAG has worked as well as is possible for a voluntary body to work". Nevertheless he thought that the Health and Safety Executive would be a much more appropriate body than the DHSS to manage DPAG's affairs. "We want everyone to know the dangers of the leaky labs", he said.

Dr Roger Nourish, microbiological inspector with the HSE, told the meeting of his visits to research and diagnostic laboratories designed to handle category A pathogens. Of the research laboratories, those at Reading and Paddington had stopped work before the HSE's visit, those at Purbright and Elstree were asked to stop work after the visit until improvements could be made and those at Porton Down and Liverpool were asked to make some improvements while still remaining operational.

Judy Redfearn

news in brief

US Supreme Court to rule on whether living organisms can be patented: The US Supreme Court agreed last week to rule on whether patents can be granted on living organisms. The case concerns two patent applications initially rejected by the US Patent Office, but subsequently granted by an appeals court. The patent applications have been filed by research scientists with the companies General Electric and Upjohn respectively; one is for an organism which is capable of breaking down oil spills, the other for a bacteria to produce the antibiotic lincomycin.

The Patent Office, supported by the Department of Justice, contends that living organisms are not covered by current US Patent Law; in support of its claim, it quotes the fact that Congress felt it necessary to pass a separate act to allow the patenting of plants. The Appeals court, however, agreed with the applicants that what was being requested was patent protection for a novel chemical process, and that this comes within the scope of the law as it is now written. In contesting the appeals court ruling to the Supreme Court, the Department of Justice argues that the economic implications of the ruling "are very significant, given the vast area that it opens to patentability."

MIT joins banking firm to study commercial aspects of applied genetics: The Massachusetts Institute of Technology announced last week that it had received a grant of \$50,000 from the US Congress' Office of Technology Assessment to co-operate with the New York banking and investment firm F Eberstadt and Co to look at the industrial and commercial aspects of applied genetics. The purpose of the grant, which will be administered through MIT's department of nutrition and food science, is to provide OTA with data for providing Congress with policy options on regulation, taxation, patent protection and research funding in the food, chemical, and pharmaceutical industries that develop and market new products and processes from living cells.

In announcing the grant, MIT said that after completion of the study, it was planned to hold a seminar for academic and industrial scientists and engineers, and for investors on the development of the industry under study. Five aspects of the industry will be covered in the study: historical development, current and predictable state of the art of various genetic technologies, research efforts in the development and applications of these technologies, and assessment of technical, institutional, economic and social factors that could affect the rate of adoption of these technologies.

French committee formed on recombinant DNA technology: A committee for information on genetic manipulation held its first public meeting 22 October at the Museum of Natural History in Paris. The meeting stressed the need of not acceding to what it called "the giddiness of biologists" and to the "fascination that genetic manipulation exercises on its practitioners". The committee hopes to call attention to the risks inherent in the new technology and to "the great laxness that exists in the definition of health and safety regulations in the area". The Secretary of the group is Jean Deutsch of the Genetic Research Group of the University of Paris VI.

Fewer US physicists means better job prospects: The employment outlook of US physicists is improving, according to a study published by the physics manpower panel of the American Physical Society. In an extensive survey of immediate past and future employment prospects for PhD physicists, the panel says supply is beginning to approach demand, and it concludes that "the physics community, taken as a whole, has passed through its gravest hour."

However the panel goes on to warn that the prime reason the job market is beginning to look healthier for new entrants is that there are so few of them. "There will continue to be imbalances between many components of supply and demand", it warns.

According to statistics prepared for the panel, the probable number of physics doctoral graduates will coincide with the total demand — assuming a 1 per cent annual growth in the table — around 1984. "*The Transition in Physics Doctoral Employment 1960-1990*". The American Physical Society, \$5.00.

Salam gives Nobel prize money to fund Third World Science: Professor Abdus Salam, co-winner of this year's Nobel Prize in Physics has pledged his share of the prize money — \$60,000 — to an international talent fund for young scientists. Speaking at a meeting of the Executive Board of UNESCO, Salam urged increased support for Third World science training because of the failure of the UNCSTD talks last August in Vienna. The developed nations, at Vienna, were asked to contribute \$2bn to aid research but had offered only one seventh of that.

Indo-Soviet scientific cooperation to expand: Indo-Soviet cooperation on science and technology will soon cover several new areas. Russia will share with India its experience and technology in earthquake prediction, laser applications, semiconductors and systems analysis over three years beginning 1980, according to a decision taken by the Indo-Soviet subcommission on science and technology which met at Moscow in the second week of October. The areas identified for cooperation in basic sciences are crystallography, low temperature physics, chemistry of natural products, microbiology and radio astronomy. The subcommission will meet again in February 1980 at New Delhi to finalize the objective in each area, time schedule and the participating laboratories.

The two sides have also decided to continue cooperation in alternative sources of energy, MHD generators, metallic corrosion, powder metallurgy, meteorology, low-cost housing, construction technology, scientific and technical information systems, machine tools, and water resource management. Earthquake prediction was included at the insistence of Professor M G K Menon, the leader of the Indian side, since the excellent system developed by the Soviet scientists for predicting and identifying the epicentre of an impending earthquake is of great relevance to the quake-prone Indo-Gangetic plain and eastern India. — S. Arunachalam.

Michigan PBB suit settled out of court: The Velsicol Chemical Corporation has made an out-of-court payment of \$2.6 million in damages to 70 Michigan farmers who filed suit against the company after buying animal feed which had been contaminated by polybrominated biphenyl (PBB). Millions of farm animals died or had to be slaughtered as a result of the contaminated feed. Velsicol also agreed to waive the farmers' debts to the farm cooperatives that sold the feed, and the farmers agreed to waive any claims of personal injury. According to Velsicol, the latest settlement clears up half of the property claims against the company. There are still 69 suits outstanding.

French government to start Tricastin 1 reactor: The French government has proceeded with the loading of its Tricastin 1 reactor in spite of the presence of cracks in the tubular collar separating the primary and secondary cooling circuits. The decision follows the one taken last week in which the Gravelines 1 reactor was started in spite of similar cracks. Both reactors had been closed because of militant trade union and community response. At this time the Communist trade union federation the CGT has decided not to oppose the loading while the Socialist federation, the CFDT has temporarily postponed further strike action. In the meantime a civil court in Paris has ruled in the government's favour in a civil suit brought by Friends of the Earth. The court ruled that it was incompetent to decide whether to grant a request by Friends of the Earth to halt the start up until the cracks are repaired or the plates are replaced.

The Asian Institute of Technology celebrates its 20th anniversary this year. David Bousfield and Ziauddin Sardar have visited it recently and have returned with different views on the impact it is making on the regional development of Asia. Here they discuss their impressions.

Could AIT be a model for the Third World . . .

THE role science and technology should play in developing countries may well be epitomised by the approach adopted by the Asian Institute of Technology (AIT) situated in Thailand about 40 Km north of Bangkok.

More than half the world's population live in the countries served by the AIT and for the past twenty years it has been gradually building up scientific and technological knowhow in the developing nations of the East. The recent UNCTSD conferences left many scientists confused as to the role they could and should play in aiding development in the Third World — the example set by AIT may help them and their governments to see a way to help.

The Asian Institute of Technology started life in 1959 as the South East Asian Treaty Organisation (SEATO) Graduate School of Engineering — the brain child of Pote Sarasin, the first Secretary General of SEATO, and a former Prime Minister of Thailand. Intended to provide a source of highly qualified engineers for Asian projects, the school began as a small collection of rooms in the Engineering Faculty of Chulalongkorn University deep in the heart of Bangkok. But it grew rapidly and in 1967 became autonomous from SEATO. Six years later it moved to its present rural setting in a 400 acre campus donated by the Thai government.

Educationally the main emphasis is on a five term master's degree in engineering or science, but PhD's are also an important part of the range of qualifications AIT can offer. At present the institute has 500 students and 62 full-time teaching and research staff. In both cases the range of nationalities is huge but most students are from Thailand itself or neighbouring countries such as Malaysia, the Philippines, Pakistan, India and Bangladesh. 60% of students who receive an AIT qualification return to their own countries to work in industry, government or universities. The institute clearly supplies a 'local' need.

Recently AIT has been gradually shifting from a strict commitment to infrastructural engineering to new fields which directly contribute to the process of national development in a Third World context. Areas such as food production, resources management, rural, industrial and urban development have become major concerns. The Divisions of Human Settlements is particularly active in this area and I spoke to Paul Vorratnchaiphan, a research associate, about one of the division's main interests, the Building Together Project.

The continual migration of rural folk to

urban areas creates many problems for developing countries. To house people properly will require considerable changes in current low-income housing policy and, consequently, research into developing appropriate low-cost housing technology is needed. AIT is currently supervising a slum resettlement programme involving the rehousing of 180 families at Lad Phrao on the outskirts of Bangkok. The initial land purchase, development and coordination was financed by 'Brot für die Welt', a German organisation, and SELAVIP, a 'popular' housing service based in Chile. By mortgaging the land and completed houses to the Thai National Housing Bank this initial 'seed' money should be sufficient to finance in serial fashion many similar projects.

The main structure of the houses is formed by special interlocking lightweight construction blocks designed by AIT and made from a rice husk aggregate in a cement and sand mix produced on site. The prospective owners, working in groups on clusters of 16-20 houses, manufacturing all the component parts themselves. Each group is broken down into teams making joists, doors, piles or casements, etc. Seventeen weeks of part-time work are required from start to finish and by this time many of the previously unskilled owners have learnt their first trade. It is hoped that this will provide some of them with a new source of income and give a better sense of purpose and cohesion to the community.

Other AIT projects include the development of a system using composted human and animal waste as a nutrient source for freshwater algae and, ultimately, fish such as *Tilapia*.

I also spoke to Robert Exell, Associate Director of the Division of Energy

Technology. Renewable energy resources are another important focus for AIT's research activities. Drying of crops, fish and meat are all long known applications of solar energy and one recent development is a solar powered rice dryer. This simple device draws air heated by the sun through a closed drying compartment containing the grains. These are protected from the rain by plastic sheeting on a bamboo framework. Half a ton of paddy rice can be dried in one to three days.

The same group has also developed a solar powered refrigerator for storing labile medical supplies in remote areas. AIT, however, hopes that the unit can also be made to provide a source of income for these communities. For example, it could be used to preserve commercially grown flowers during the critical period between cutting and refrigerated export to Hong Kong. AIT is currently collaborating with a local university project aimed at introducing this refrigerator and flower culture into the economies of primitive hill tribes in the north.

I spent a day on the AIT campus and only managed to visit two research wings. In fact the institute has nine teaching and research divisions, these being agricultural and food engineering, computer applications, environmental engineering, geotechnical and transport engineering, human settlements development, industrial engineering and construction, water resources engineering and, the most recent addition, energy technology. Also, the institute is the home of the South East Asian regional computer centre, one of the best engineering libraries in South East Asia, a language and media centre (the language used by the institute is English) and the Regional Documentation Centre.

David Bousfield



AIT's low-cost, appropriate housing for slum resettlement

... or does the West have too much control?

THE Asian Institute of Technology (AIT) advertises itself as a centre of excellence which "provides opportunities for men and women of diverse Asian nationalities to study and work together to seek, define, and test technological solutions to the common problems affecting the quality of life in Asia". This claim is indeed partly justified; but the institute's impact on Asia, as a whole, has been negligible.

AIT's approach to the problems of Asia is based on the belief that academic excellence can be integrated with teaching and research for appropriate solutions to Asian problems. This approach has largely paid off and AIT can justly claim that its graduates are tailor-made for Asia's needs and that as a post-graduate technological institute it has produced over the past two decades, a small cadre of technocrats that now occupies key positions in Asia's private sector.

On the research front too, most AIT projects are based on problems of practical importance relevant to Asia's development. In their own way, some of these projects, such as integrated farm study, a small scale fishery project, slum settlements and flood forecasting studies, have made significant contributions at local level.

However, from a general regional perspective, AIT's contribution to Asia seems almost insignificant. In 1977, for example, AIT graduates included one graduate from Iran, 7 from Malaysia, 12 from Pakistan, 20 from Sri Lanka and 49 from Thailand. This year, AIT's graduate output included one student from Iran, 9 from Malaysia, 11 from Indonesia, 14 from Pakistan and 16 from Sri Lanka. On this basis of graduate output almost every

technological university in the UK can claim to contribute much more to the educational development of Asia than AIT. With the exception of human settlement development, research at AIT too has failed to have a regional impact.

Indeed, both from the point of view of education and research, the chief beneficiary of AIT's endeavours is Thailand. Over one-third of AIT Alumni are Thais. Of the 15 research projects started in 1978, nine were related directly to the needs and requirements of Thailand.

AIT has considerable difficulty attracting students. Universities and colleges in many Asian countries do not know of its existence and consequently cannot recommend their graduates to apply for its post-graduate training. Even when a student applies and is accepted, political reasons may prevent him from attending. Most students who can go abroad to study would prefer to go to the West than to AIT in spite of its excellent reputation.

One reason why AIT has not made a significant impact on the region is that, even after twenty years, it is still regarded as an alien body. Even in Thailand, it is looked upon as having been transplanted from the West. In other Asian countries too AIT is thought of as non-Asian. In Pakistan, Iran and Turkey it is hard to find science policy makers at the ministerial level who do not have some reservations about it.

Part of the reason why AIT is labelled as an alien institution is that it is administered and funded largely by the West. Less than half of its 39-member Board of Trustees are Asian, and most of these are Thais with a token Malaysian, Indian, Indonesian and

Sri Lankan. Amongst AIT's major backers are IBM, Shell, Esso and Bes Engineering. Other major contributors include Canada, Japan, US, Thailand and the Ford, Rockefeller, Chase Manhattan, Readers' Digest and Starr Foundations.

On the whole, the donors keep a good eye on the institute. Visits by their representatives are frequent. Indeed, as Dr Robert Excell, Associate Director of Energy Technology Division, who has been at AIT almost a decade says, some donors tend to dictate and influence AIT's policy. This trend seems to be increasing and, according to Excell, is a major area of concern for AIT's future. "We must try and remain independent of donor influence in the future", he says.

Donor influence apart, a major future area of AIT's contribution to the region is specialised science information. AIT has an excellent Regional Documentation Centre which was set up in 1977 with the objective of improving access to information in the region and of initiating and participating in information projects on a regional basis. There are also four specialised information centres that have already proved their worth: the Asian Information Centre on Geotechnical Engineering, the International Ferrocement Information Centre, the Renewable Energy Resources Information Centre and the Environmental Sanitation Information Centre. AIT's Regional Information Centre, together with the four special information centres, could act as a regional focal point for the global information system proposed by UNCSTD (*Nature* 6 September page 4), if AIT can seek out users and meet their needs.

Ziauddin Sardar

US strengthens scientific links with Latin America

Closer scientific links between the US and various Latin American countries are expected to follow a visit made last month to four countries by a top level team of science policy makers, headed by the President's science adviser, Dr Frank Press.

The delegation stressed that the purpose of the visits was directly in line with the agreements reached at the United Nations Conference on Science and Technology for Development in Vienna in August. "I was very pleased with the trip — the response was very warm and positive", Dr Press told *Nature*.

The visit also helped to prepare the ground for US strategy at the annual meeting of the Organisation of American States, which opened in Bolivia recently, at which the US is keen to promote technological and economic cooperation between Latin American countries as a way of promoting political stability on the

entire American continent.

During the visits to Peru and Barbados, for example, the US delegation met with representatives of the two regional organisations, the Andean Pact, and the Economic Pact between Venezuela, Ecuador, Peru, Colombia and Bolivia — and the Caribbean Community Secretariat (CARICOM).

During the visit to Peru, the delegation met officials of the Junta del Acuerdo de Cartagena, the secretariat for the Andean Pact, to emphasize its willingness to support research programmes initiated by the Junta aimed at increasing technical collaboration between the five countries (see *Nature*, 12 October 1978).

The delegation's visit to Venezuela was aimed primarily at strengthening scientific links which already exist with the US. Particular attention was paid to proposals from the Venezuelan side on developing cooperation in basic and applied scientific

research, particularly in the fields of marine biology, neurobiology, electronics and hydrology.

In Brazil, it was more a question of rebuilding links that have been strained in recent years. Here the specific topics under discussion included coal liquefaction technology, long-distance energy transmission by superconductors, and establishment of a diagnostic reference centre, as well as industrial technology and inter-university science and technology cooperation.

During the visit to Barbados, the delegation met with representatives of other regional development and research organisations. A communiqué issued after the meeting said that "the two sides expressed satisfaction with the progress made in the limited time available towards establishing a sound basis for science and technology cooperation between the United States and the Caribbean". □

correspondence

Human ingenuity is wasted on nuclear power

SIR,—I rather hoped that "nuclear nonsense" might draw a response from UKAEA. It is not nonsense that fast reactors produce 60 times more energy than thermal reactors. I said in my original letter (13 September, page 98) that it might be true in 200 years' time. Cutts and Smith (18 October, page 522) admit that it could not come about until after all thermal reactors had been replaced by fast reactors, and that on the best figures UKAEA could produce the ratio would only be 1.7 by 2020; so as they do not give a figure of their own, I take it that 200 years is not unreasonable.

What is nonsense is the use of this hypothetical long term ratio of 60 as an argument for developing fast breeder reactors now. It is all the more nonsensical because Granger and Merrick showed that even a delay in starting a fast breeder programme of as much as 30 years would be rapidly made up, because the main limiting factor is the production of plutonium by thermal reactors.

This is implicitly admitted by Cutts and Smith, because having predictably taken my "nuclear nonsense" to refer to the 60 times ratio, rather than Smith's use of it to support the development of fast breeder reactors, they then drop this argument and concentrate on lauding the possibility of eventually reducing uranium imports to zero. On this basis coal would seem to be a clear winner for the medium term, and the long term superiority of conservation plus solar energy over both hardly needs demonstrating.

It is an amazing paradox that nuclear scientists and technologists — even Alvin Weinberg (4 October, page 335) — can claim that human ingenuity is so great that it can deal successfully with all the problems which are associated with Three Mile Island and the 'China Syndrome', in a world dotted with nuclear reactors and repositories of highly radio-active waste requiring protection for thousands of years, a world in which the use of nuclear energy will inevitably be accompanied by the widest proliferation of nuclear weapons. Yet when faced with the job of utilising just one hundredth of one per cent of the energy showered on us by the only safe nuclear power plant — the Sun — human ingenuity flies out of the window, and only the difficulties can be seen. Yet this latter use of human ingenuity is the only one which offers even a glimmer of hope for the future of mankind.

Yours faithfully,

J. W. JEFFERY

Birkbeck College, University of London, UK.

Aflatoxin B₁ in barley in the UK

SIR,—In the United Kingdom in the early 1960s a link between the death of 100,000 turkey poult and the fungus *Aspergillus flavus* was recorded. Further studies identified the toxic entity of the fungus to be aflatoxin B₁, produced in imported groundnut. Further research led to the detection of aflatoxin in many animal and human feeds imported into the United Kingdom, e.g. walnut, pistachio, maize, cotton seed, etc.

Though *A. flavus* has been isolated in the UK, it has been thought either that strains are

not capable of producing aflatoxin B₁, or that the substrate and conditions are not conducive to aflatoxin B₁ production. In June of this year, however, a farmer requested advice from Microbiology Department of the Ministry of Agriculture, Wales on the health risk to himself or his stock from mouldy barley. Enquiries found the barley had been treated with commercial propionic acid at an inadequate application level. Further laboratory examinations showed the mould to be *Aspergillus flavus* (5×10^7 prepaques/g barley), while mycotoxin examination gave a level of 125 µg aflatoxin B₁/kg barley.

The detection in a home grown cereal of aflatoxin must be regarded with some concern, because of its known carcinogenic and toxic properties. Also, questions must be asked as to the significance of a chemical additive. Additional studies are to be carried out to place this finding in perspective. We intend to study *A. flavus* isolates from soil and grain in Wales, for their ability to grow in varying concentration of propionic acid, and also, to assess such isolates for aflatoxin B₁ production. The results should help to clarify whether this incident is an isolated case or part of a greater problem.

Yours faithfully,

A. HACKING
N. R. BIGGS

Welsh Office, Aberystwyth, UK.

Cooperation with the USSR

SIR,—I have read the letter from Lee Lorch (13 September, page 98) with great concern. He does not seem to realize that cooperation must be two-sided; to be accepted as an equal partner, the Soviet Union must treat all its nationals on an equal footing.

Admittedly, the West may lose as much as the USSR by reduction of cooperation. But what other way is there of protesting against the way that the USSR is treating its Jewish scientists?

Yours faithfully,

H. LIPSON

University of Manchester Institute of Science and Technology, UK.

Wartime research on nitrogen mustard

SIR,—Thirty seven years ago the late Major J. M. Moore of the USA and I carried out classified experiments on the influence of nitrogen mustard — then a secret compound — on the bone marrow stem cells. Dameshek¹, Gilman² and Harrison³ have commented on work prior to 1945 as being classified but important in the evolution of the treatment of leukaemia and cancer. Colleagues in Melbourne have suggested that for historical reasons we should have our work carried out in 1942 declassified and published.

During the first world war mustard gas exposure in man was found to be associated with leukopaenia. This was believed to be due to superadded infection; it was not recognised that it was due to a chemical effect on the bone marrow.

In 1942 we tested the effect of nitrogen mustard on the bone marrow. We selected guinea pigs and compared the cellular distribution in bone marrow in a series of

control animals against that of a series of similar animals exposed to the vapour of nitrogen mustard. Red marrow from the upper end of the tibia was examined. We found both the cells of the myeloblast series and the lymphoblast series were highly significantly reduced in numbers. This information was supplied to both the Ministry of Supply, London and also to Washington at that time. It is interesting to note that at that time much doubt was expressed that lymphocytes actually developed in bone marrow. This work was done in my laboratory at the University of Melbourne.

The Australian Defence Research Laboratory recently told me that there was no difficulty in obtaining security clearance for this work which was now common knowledge — but they were not able to find the documents recording the research of the "Gorrill" chemical warfare research team.

Our experiments on chemical warfare agents were essential to the war effort both owing to the capability of the Japanese in chemical warfare and the world ignorance of the precise effect of these agents under tropical conditions as applied to New Guinea. Unfortunately some years after the war, a directive was made that all documents relating to this work by the "Gorrill team" — later under the direction of another commanding officer — were to be destroyed. The senior official who destroyed them told one of us he thought he might have been destroying significant scientific material. Under security wartime arrangements neither of us had copies of this document.

Yours faithfully,

E. R. TRETHERWIE

Walter and Eliza Hall Institute of Medical Research, Victoria, Australia.

1. Dameshek Blood, 4, 338, (1949).
2. Gilman Science, 103, 140, (1946).
3. Text Book of Medicine, Harrison, p. 1787 (McGraw-Hill, New York, 1977)

Obstructionists in environment clothing

SIR,—After its sincere start, "The end of the age of Aquarius?" (20 September, page 168) has been brought about in part by the duplicity of some so-called

"environmentalists", who are, in fact, merely obstructionists. The writer personally investigated an attempt by such a group to include in the Organic Act, governing the US Bureau of Land Management, the setting aside of several square miles of rich coal lands in southern Utah as a sanctuary for the side-blotched uia, *Uta stansburysensis*. This small, brown lizard, with its subspecies, is common in suitable habitat over most of the Desert Southwest, from western Colorado to eastern California and is by no means in danger of extinction. Only the alertness of a US Senator from Nevada thwarted the move.

Even the discovery of the snail darter as an endangered species appears to have been based on an effort to block the construction of the Tellico dam, and not *vice versa*. Thus do the over-zealous and ulterior motivated subvert worthy endeavour, with the result that the efforts of the reasonable and sincere are eventually largely nullified.

Yours faithfully,

S. RALPH AUSTIN

Grand Junction, Colorado

news and views

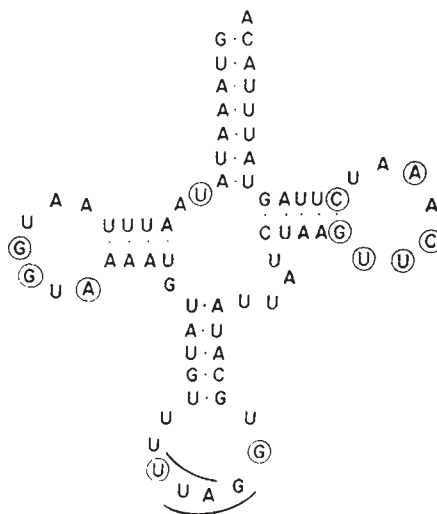
Mitochondria spring surprises

THE concept of a totally universal genetic code was based initially on studies of *E. coli*, tobacco mosaic virus, and human haemoglobin. The extrapolation of this conclusion from three genetic systems to all organisms was justified by the theoretical premise that any mutation which changed the ancestral code would cause so many different deleterious effects that it would have been selected against. Impressive though this argument may be, eukaryotic mitochondria have not heeded it. DNA-protein sequence comparisons for mitochondrial genes have revealed three variant codon assignments, at least one of which (UGA coding for tryptophan rather than acting as a termination codon) is used both in human and in yeast mitochondria.

An extraordinary skewing of the mitochondrial codon usage pattern in favour of codons ending in A and U and away from those ending in G and C was evident from the first complete mitochondrial gene sequence determined, that for yeast ATPase subunit 9 (Hensgens *et al.* *Proc. natn. Acad. Sci. U.S.A.* **76**, 1663; 1979). For other yeast mitochondrial genes this same pattern holds, while for the single mammalian mitochondrial gene sequenced, only triplets ending in G are particularly infrequent.

B. D. Hall is a Professor in the Department of Genetics, University of Washington, Seattle.

(Hensgens *et al. op. cit.*; Macino & Tzagoloff *Proc. natn. Acad. Sci. U.S.A.* **76**, 131; 1979), which normally codes for leucine. Follow-up sequencing studies established that the apparent discrepancy was due neither to a sequencing error nor to a genetic polymorphism. A structural basis for assignment of the CUA codon to threonine can be deduced from the sequence of an unusual yeast mitochondrial tRNA gene. Li and Tzagoloff have found (*Cell* **18**, 47; 1979) that a yeast mitochondrial DNA fragment which hybridises to tRNA^{Thr}_{mt} contains a single tRNA gene sequence, that shown below



This sequence differs from all previously-analysed tRNA sequences by having eight rather than seven nucleotides in the anticodon loop. Within this loop, the two nucleotide triplets nearest the centre are complementary to the nonsense codon UAA (overlined sequenced) and to CUA (underlined sequence). The mitochondrial tRNA transcribed from this gene may therefore be capable of accepting threonine and inserting it opposite the CUA codon triplet in ATPase subunit 9 mRNA and perhaps also at other CUA codons in mitochondrial mRNAs.

The second exceptional feature of the mitochondrial genetic code was discovered by similar protein — DNA sequence

These strange goings-on in human cytochrome oxidase are not unique to our species. T. Fox of Basel University (*Proc. natn. Acad. Sci. U.S.A.*, in the press) has obtained very similar DNA sequence results for the yeast *oxi1* locus, a mitochondrial gene which codes for yeast cytochrome oxidase subunit 2. The amino acid sequence of yeast COII decoded from the *oxi1* DNA sequence, is 38% homologous to that of the bovine COII protein. This yeast gene, like its human counterpart, can only be translated to make COII protein if UGA codons are read as sense. Out of five TGA triplets in *oxi1*, four occur at positions where the bovine protein contains tryptophan. Similar conclusions were reached in an earlier publication which reported a partial DNA sequence for *oxi1* (Macino *et al. Proc. natn. Acad. Sci. U.S.A.* 76, 3784; 1979). These authors raised the possibility that UGA also is read as a sense codon in two other yeast mitochondrial genes, *oli2* and *box4*.

As a third possible variation, Barrell *et al.* (*op. cit.*) note that in mitochondria AUA may code for methionine, rather

than isoleucine. From an alignment of the bovine COII amino acid sequence with the sequence of codons in the human COII gene, they observed that methionines occur opposite ATG at two and opposite ATA at five positions. Provided there was no large scale evolutionary interconversion of isoleucine and methionine codons it would appear that AUA codes for methionine in human mitochondria. There is not yet enough protein sequence data to determine whether AUA also codes for methionine in yeast mitochondria.

The structural grounds for the AUA to Met and UGA to Trp codon assignments are presumed by Barrell *et al.* to be nucleotide bases present at the wobble positions in the anticodons in tRNA^{Met}_{mt} and tRNA^{Trp}_{mt}. The presence of U or modified U at the 5' end of the anticodon in each case might allow translation of AUA and UGA by A-U base pairing and of AUG and UGG by wobble base pairing (Crick, *J. molec. Biol.* 19, 546; 1966). Recent sequencing work by Sanger and Coulson (cited by Barrell *et al.*) has established that the anticodon of human tRNA^{Trp}_{mt} has a sequence consistent with these postulates.

These variations of the mitochondrial genetic code from that which directs translation in *E. coli* illustrate that, once a genetic code came into existence, it was not immutably fixed in all its details. Will still more exotic variations in the code be found in other organisms? For the answer, consult the dictionary in your favourite dinoflagellate, protozoan or archaeobacterium. □

Antimatter from space

from P.C.W. Davies

THE origin of matter is one of the great unsolved problems of science: the visible Universe contains about 10^{50} tons of material. Where did it come from? At one time it was supposed that all this cosmic stuff — from which the galaxies, the stars and our own bodies are made — always existed. Modern cosmologists, however, believe that the Universe is not of unlimited age, but came into existence about 15 billion years ago in the hot, dense, explosive eruption, popularly called the big bang.

If this primaeval explosion marked the creation of all the cosmic matter, physicists would like to understand the details: what precisely happened in the first microsecond of existence? Since the early 1930s it has been known that matter can be created

from energy in the form of subatomic particles, so modern cosmology provides a natural mechanism for the origin of matter: it was created from the explosive energy associated with the primaeval violence. Paul Dirac gave a very heuristic explanation of how this happens. The equation that describes a particle such as an electron possesses two sets of solutions: one describing 'ordinary' electrons and the other mysterious states in which electrons have negative mass-energy. As all systems tend naturally to seek out their lowest energy, nothing apparently prevents ordinary electrons from descending into these enigmatic negative energy states. As the energies can be limitlessly negative, there is a sort of bottomless pit into which all matter can disappear amid a shower of energy.

To preclude this apocalypse, Dirac proposed that the pit is blocked with an infinity of invisible electrons. If one of these invisible negative energy electrons is given enough energy it will be promoted to a real, observable, positive energy electron. Thus, a new electron will suddenly materialise in space. Furthermore, the 'hole' left behind represents the absence of an invisible negative energy electron, which Dirac reasoned is equivalent to the presence of a visible positive energy anti-electron, or positron as it is now called. The positron is a sort of mirror image to the electron; like the latter, but with all its physical attributes (for example, charge, spin, magnetic field) reversed.

Positrons were discovered among cosmic ray debris in 1932, and since then, antiprotons, antineutrons and a host of other antiparticles have been identified. Until recently it was supposed that the creation of matter must always be accompanied by an equal quantity of antimatter of the corresponding type. This inevitably implies that for every atom of ordinary matter that we see, somewhere in the Universe lurks its opposite number. Because any contact between matter and antimatter results in the matter falling back into the 'holes' and disappearing from the Universe, it must be supposed that somehow the matter and antimatter have got themselves well separated. It is fashionable to suggest that there are whole galaxies made of antistars and antiplanets and, one may conjecture, antipeople. An antigalaxy would look, on the face of it, indistinguishable from an ordinary galaxy.

When matter and antimatter annihilate each other their mass gets converted back into energy in the form of gamma rays, so by measuring the flux of gamma rays from space, limits may be placed on the amount of mixing that occurs between the two species of material. This seems to imply that almost complete separation has occurred, even on the scale of galactic clusters. Presumably they were put asunder in the earliest epochs of the big bang but just how this could have happened is still not completely clear.

In the past few years an exciting alternative picture has emerged. Ambitious new theories that seek to unify three of nature's four forces into a single mathematical description have predicted that perhaps matter can be created without an exactly compensatory quantity of antimatter. If this is so, it opens up the possibility of a lopsided Universe in which most of the antimatter has been annihilated, leaving a small residue of unbalanced matter that constitutes all the observed Universe.

To test which of these theories is closest to the truth, physicists can search for antimatter in space. Although the nearest antigalaxy may be millions of light years away, perhaps high energy subatomic antiparticles can stream across the gap and pepper the Earth. Cosmic ray showers have long been known to contain some antimatter (that is how the positron and antiproton were first discovered), but it has not hitherto been known whether these are merely by-products of high energy collisions between ordinary particles among the cosmic rays and the Earth's upper atmosphere. Now an experiment has been performed by a group of physicists from Texas and New Mexico to search for antiprotons among the primary rays (*Phys. Rev. Lett.* 43, 1199; 1979). From a high altitude balloon flight last 21 June, the group detected 46 such particles, of which only about 18 are attributable to reactions with the atmosphere.

The ratio of antiprotons to protons coming from space works out at 5×10^{-4} in the energy range explored, which accords well with theoretical estimates based on the assumption that no external flux of antiprotons is bathing the Galaxy. They can all be accounted for as by-products of collisions between ordinary cosmic rays and the tenuous interstellar medium in deep space.

This experiment not only provides important information for understanding the origin and behaviour of cosmic rays in the Galaxy, but it tightens up further the evidence against a matter-antimatter symmetrical Universe. If matter really can be created and annihilated alone, it will open up whole new chapters in both cosmology and subatomic physics. □

100 years ago

In his last report from Saigon, Mr. Consul Tremlett alludes to his having been ordered by the Foreign Office to procure and send home a quantity of the bark known as *hwang-nao*, which during the past four or five years has been exported from Tongking to Trinidad, and there seems to have proved efficacious in cases of leprosy. The tree from which it is obtained is hardly known except to the missionaries, and is only found in the mountain forests of the north of Annam.

From *Nature* 21, 6 Nov., 19; 1879.

P.C.W. Davies is in the Department of Mathematics, King's College, London.

The road to unification

Sheldon Glashow, Abdus Salam and Steven Weinberg have won the 1979 Nobel Prize for physics for their great contributions to a unified theory of two of the fundamental forces of nature — the weak and electromagnetic interactions. But the theory took a long time to develop, and in that time many physicists other than those who were awarded the final accolade also made important contributions to it. On the next page Robert Walgate outlines the background of the theory and Norman Dombey traces here, for the initiated, the history of the Glashow-Salam-Weinberg model.

THE award of the Nobel prize in physics last week to Glashow, Salam and Weinberg can be seen as marking the end of the second phase of post-war theoretical particle physics. The first phase, which lasted until the mid-1950s was concerned with the development of quantum electrodynamics (QED) and is associated with the names of Tomonaga, Schwinger, Feynman and Dyson. The second phase begins with the discovery in 1957 of the non-conservation of parity in weak interactions — the interaction responsible for the neutron beta decay $n \rightarrow p e^- \bar{\nu}$ and muon decay $\mu^- \rightarrow e^- \bar{\nu} \nu$ — following its prediction by Lee and Yang¹.

After this, there was rapid progress in the understanding of weak interactions. Fermi² had written down a contact coupling of the four fermions involved in beta-decay in 1933 and for over 20 years it was the task of experimental nuclear physicists to work out the details of that coupling. The parity experiments then fixed the Fermi coupling as a current-current coupling of the neutron-proton or muon-neutrino current to the electron-neutrino current. (Current here has the technical meaning of behaving like a vector plus axial vector under Lorentz transformations.) Furthermore, the experiments showed that the strength of the vector part of the Fermi coupling G_V for beta-decay was almost precisely the same as G_μ for muon-decay.

A possible explanation for this was given independently by Gershtein and Zeldovich⁴ and Feynman and Gell-Mann³. If the vector current of weak interactions were conserved, irrespective of whether it involves the strongly-interacting hadrons (nucleons, pions and so on) or only involves the leptons $\mu^\pm, e^\pm, \nu$ which have no strong interactions, then as in electrodynamics there is an associated conservation law. So in place of charge conservation, which leads to the equality of the electric charge of the proton and e^+ , there is the weak 'charge' equality $G_\mu = G_V$.

Once this was accepted as a serious possibility, there was a clear analogy between the electromagnetic and weak interactions as both involved a conserved current and both were universal in that they involved leptons and hadrons with equal strength. There are of course many important differences: the characteristic strength of weak interactions is given by G_V where $G_V m_p^2 \approx 10^{-5}$ (m_p is the proton mass) whereas the equivalent strength of

electromagnetic interactions is given by the fine structure constant $\alpha \approx 10^{-2}$; electromagnetic interactions conserve parity whereas weak interactions violate it maximally; electromagnetic interactions are long range whereas weak interactions act at a point; and so on. Using the analogy, Schwinger⁵ in 1957 wrote down a unified weak-electromagnetic interaction based on the Yang-Mills⁶ generalisation of QED. This involved a triplet ($\gamma^+, \gamma^0, \gamma^-$) of charged photons: the theory conserved both charge and isotopic spin and thus provided a dynamical basis both for isotopic spin conservation and for the connection between charge and isotopic spin. Unfortunately, no zero mass charged photons have ever been seen.

Nevertheless, Yang-Mills theory does lead to a conserved vector current with charged components and that is precisely what is required for weak interactions. Schwinger had to assume that there was some mechanism by which the charged photons $\gamma^\pm$ acquired a very heavy mass so as to simulate the pointlike character of the weak interaction: these were to become known as the intermediate vector bosons $W^\pm$ of the weak interaction. If this mass M_W satisfied $G_V M_W^2 \sim \alpha$, that is $M_W \sim 30$ GeV, then the resultant weak-electromagnetic interaction was unified in the sense that now α represented the coupling strength of both interactions. From this viewpoint, the reason that weak interactions were so weak was simply because the $W^\pm$ were so heavy that they were unlikely to be exchanged at the energies characteristic of nuclear physics. The properties of this theory were further developed by Schwinger's student Glashow⁷ and Salam and Ward⁸ during 1958.

Not many physicists took these early papers seriously as the parity-violating aspects of the charged weak current were completely unexplained and difficult to reconcile with the parity-conserving electromagnetic current. The first paper which made real progress was published by Glashow⁹ in 1961 and provides the foundation of the present theory. Glashow showed that the parity properties of the electromagnetic and weak currents were possible to reconcile in terms of the known leptons provided that a triplet (W^+, W^0, W^-) of vector bosons coupled to the left-handed leptons while a fourth vector boson B^0 coupled to both left and right-handed leptons. Then quantum mixing between B^0 and W^0 gave rise to the physical states — the photon γ and a predicted neutral vector boson Z^0 . In this way it was possible to

arrange that the photon coupled equally to left and right handed leptons thus conserving parity whereas Z^0 coupled unequally. So in this $SU(2) \times U(1)$ theory (the technical name of the underlying group), there was a new neutral weak current coupling to Z^0 which violated parity in a predictable non-maximal way. Glashow's work was followed in 1964 by an independent derivation of essentially the same result by Salam and Ward¹⁰, who surprisingly were unaware of Glashow's work. The main difference between the two approaches is that Glashow has two left-handed doublets (ν_e, e^-), (ν_μ, μ^-) to describe the leptons whereas Salam and Ward preferred the group $SU(3)$ and took the basic lepton triplet (μ^+, ν, e^-) with a 4-component neutrino instead of two 2-component neutrinos ν_e, ν_μ . Salam and Ward's choice allows certain possibilities absent for Glashow such as a neutrino magnetic moment and *vice versa*, but there is no necessary difference between the theories.

These early papers give most of the results of the present theory when applied to leptons. Nevertheless, the theories were not renormalisable: unlike in QED it was not possible to calculate higher order effects in the coupling constant α . The problem of calculating with massive vector bosons (that is spin -1 particles) had been known for many years. Such particles can have their polarisation vector either perpendicular (transverse) or parallel (longitudinal) to their direction of motion. A zero mass, spin -1 particle can by Lorentz invariance only have transverse modes but a massive vector boson must have the longitudinal mode too. The problem arises because the longitudinal polarisation vector has a component proportional to the momentum vector k_μ ; hence the probability of emitting (or absorbing) the particles in their longitudinal mode will increase both with particle momentum/energy and with

1. T D Lee and C N Yang, *Phys Rev* **104**, 254 (1956)
2. E Fermi, *Ric. Scientifica* **4**, 491 (1933)
3. S S Gershtein and Y Zeldovich, *JETP* **29**, 698 (1955); (English translation *Sov. PL. JETP* **2**, 576 (1956))
4. R P Feynman and M Gell-Mann, *Phys Rev* **109**, 193 (1958)
5. J Schwinger, *Ann Phys* **2**, 407 (1957)
6. C N Yang and R L Mills, *Phys Rev* **96**, 191 (1954)
7. S L Glashow, *Nucl Phys* **10**, 107 (1959)
8. A Salam and J C Ward, *Nuovo Cim* **11**, 568 (1959)
9. S L Glashow, *Nucl Phys* **22**, 579 (1961)
10. A Salam and J C Ward, *Phys Lett.* **13**, 168 (1964)
11. A Salam, *Nucl Phys* **18**, 681 (1960); *Phys Rev* **127**, 331 (1962)
12. Y Nambu and G. Jona-Lasinio, *Phys Rev* **122**, 345 (1961)
13. F Englert and R Brout, *Phys Rev Lett.* **13**, 321 (1964)
14. P W Higgs, *Phys Rev Lett.* **13**, 598 (1964)
15. S Weinberg, *Phys Rev Lett.* **19**, 1264 (1967)
16. A Salam, 'Elementary Particle Theory', ed N Svartholm, Stockholm 1968, p367
17. S L Glashow, J Iliopoulos and L Maiani, *Phys Rev D*, **12**, 1285 (1970)
18. G 't Hooft, *Nucl Phys* **B33**, 173 (1971); **B35**, 167 (1971)
19. F Hasert et al. *Phys Lett.* **46B**, 1381 (1973)
20. C Prescott et al. *Phys Lett.* **77B**, 347 (1978)

Norman Dombey is in the Department of Physics, University of Sussex

the number of particles emitted. This is not possible in a sensible renormalisable theory which should give finite results at all energies and for any number of particles. In renormalisable theories all processes to any order in the coupling constant are calculable in principle.

Salam¹¹ in particular emphasised the importance of the renormalisability criterion and thought that it should follow as in QED from a principle of gauge invariance. In QED this is the statement that the components of the electromagnetic field vector A_λ in the direction of the photon momentum k_λ are redundant. It follows just as in classical electrodynamics that the photon (or electromagnetic wave) can only possess transverse modes, thereby removing the difficulty inherent in longitudinal modes. However, for QED to be gauge invariant the photon must have zero mass. Yang-Mills theory involves a more complicated gauge invariance where the 'photons' must also have zero mass.

The problem of inducing a vector boson mass without destroying the gauge invariance of the theory was actually solved in 1964 in some seemingly obscure work based on the theory of superconductivity. In superconductivity the ground state of the system is not invariant under the full symmetry of the interaction describing the system (a simpler example is ferromagnetism where the direction of the ferromagnet in its ground state clearly breaks the rotational symmetry of the underlying spin-spin interaction); an energy gap thus appears between the ground state and the lowest symmetric state. Nambu and Jona-Lasinio¹² showed that this process of spontaneous symmetry breaking (SSB) can be considered as the generation of mass for a fermion initially with zero mass but with a pairing interaction as in superconductivity. The energy gap behaves like a mass.

Brout and Englert¹³ and Higgs¹⁴ then showed that if one starts with a gauge theory involving a zero mass vector boson interacting with scalar fields, then SSB will generate a mass for the vector boson without destroying the gauge invariance of the underlying interaction. So it is possible that the good (that is, renormalisable) properties of the underlying theory are retained. In this case at least one scalar particle must also exist as a result of SSB.

It is surprising in retrospect that it took physicists three years to incorporate the ideas of SSB into unified weak-electromagnetic theory. In 1967 Weinberg¹⁵ applied these ideas to Glashow's $SU(2) \times U(1)$ theory thereby predicting the mass relation $M_W = M_Z \cos \theta$ where θ is Glashow's mixing angle so giving the strength G' of leptonic neutral currents as $G' = \frac{1}{2} G_\mu$. Furthermore, the mass M_W is $37/(\sin \theta)$ GeV or about 78 GeV with the present value for $\sin \theta$. Salam at about the same time was applying the ideas of SSB to his own and Ward's version of the theory. His results¹⁶ are in agreement with those of Weinberg but his more general approach

What the theory is about

EINSTEIN spent the latter half of his life struggling to find a unified theory of the gravitational force and electromagnetism; he failed because he could not transfer the geometrical ideas of the general theory of relativity (his space-time theory — still the current theory — of gravitation) to the electromagnetic field. However he twisted and turned his electromagnetic 'vectors' and 'tensors' electromagnetism remained stubbornly non-geometrical: the electric and magnetic forces were something you simply had to add to space-time, like actors on a stage.

But now Glashow, Salam, and Weinberg, and the physicists who worked before and with them (see accompanying article) have turned the tables on Einstein by unifying electromagnetism with something else — the weak interaction, which is responsible for the 'beta decay' of radioactive nuclei and for the transformation of protons into neutrons (and hence hydrogen into helium) that allows the Sun to burn. Both electromagnetism and the weak force are described in the theory as fields of force laid upon space-time; but they are now conceived as aspects of the same field of force, seen in different circumstances, just as magnetism and lightning are different aspects of the electromagnetic field.

Electricity and magnetism, incidentally, were unified by the Scot James Clerk Maxwell towards the end of the 19th century, in a 'field theory' which is still very much at the root of modern theories of fields of force. Maxwell showed that there must be propagating waves of electromagnetic field, and that they would travel at the speed of light; Hertz demonstrated their existence.

Light is an electromagnetic wave radiated by moving electric charges. It follows that if the weak force is to be combined in a unified theory with electromagnetism, there must be 'weak' charges and a corresponding radiation. In particle language (corresponding to the invocation of quantum mechanics, and the 'quantisation' of the field) there are photons (for light) and what came to be known as 'intermediate vector bosons' for the weak radiation. The difference is that photons are massless, and can cause interactions at infinitely long range, whereas the IVBs are massive and cause

short-range forces. Thus the weak field of protons and neutrons cannot be felt outside the atomic nucleus whereas their electric field extends outwards and captures electrons, thus creating atoms. Inside the nucleus, the weak field causes beta decay.

So far so good, but we still only have parallel theories, not unified ones. The next step was highly technical, and took a long time to emerge, but has very interesting consequences. It proved that the weak and electromagnetic fields could be understood as aspects of the same field only if the 'uni-field' was being propagated through a physical medium, the Higgs medium spreading throughout space-time. The medium was rather like calcite, which splits light into two beams according to its polarisation; the Higgs medium splits the uni-field (which has massless, long-range particles) into a heavy part (the IVBs) and a massless remainder (light).

Back to the aether, do I hear? Not quite. The medium is supposed to be real and detectable, and it obeys all the constraints of special relativity. Since it is uniform throughout space-time it is not noticeable until it is altered locally in some way, which cannot be done except at very high particle energies; but at those energies it is possible to predict that 'Higgs particles' will be created, like splashes in the medium (they will correspond roughly to density waves like sound in air).

The theory also predicts the exact masses and charges of the IVBs (there will be three, positive, negative, and neutral); and although it has been well verified at low energies in experiments with electrons and neutrinos, the real test will come with the detection (or not!) of the IVBs and the Higgs particles. Meanwhile particle theorists are attempting to apply the techniques of Higgs media (or 'spontaneous symmetry breaking' as it is called) to a unification of the weak, electromagnetic, and strong forces — without, yet, it must be admitted, much success.

Once the experiments that test the Glashow-Salam-Weinberg model have been done we shall know whether we are on the right lines or whether we have to start along a completely new track.

Robert Walgate

did not allow him to derive explicit mass relations for M_W and M_Z .

The rest is history. On the theoretical side, Glashow, Iliopoulos and Maiani¹⁷ in 1970 introduced the concept of charm (*Nature* 262, 537; 1976) thereby allowing the unified theory to be applied to hadrons and not only to leptons; the following year 't Hooft¹⁸ showed in a *tour de force* that the Weinberg model was renormalisable.

Experimentally, weak neutral currents were discovered in the remarkable experiment²⁰ at SLAC last year (*Nature* 274, 11; 1978), when it was shown that left-handed electrons scatter off deuterons more than right-handed electrons.

In conclusion it is only fair to give credit to those whose work was inextricably linked with the development of the theory, which as is clear was very much a

collaborative effort, but whose names were not chosen at Stockholm: in particular Ward and 't Hooft. It is also necessary to add the note of caution that so far neither the vector bosons $W^\pm$ and Z^0 nor the scalar particle implied by SSB have been discovered (*Nature*, 279, 675; 1979). If the mass of the Z^0 is indeed 90 GeV as predicted, then it will be discovered in the next two or three years at PETRA in an e^+e^- experiment and at CERN in a $p\bar{p}$ experiment. If not . . . $\square$

Small-scale solar magnetic fields

from Lawrence E. Cram

OBSERVATIONAL studies of the solar atmosphere show that a large fraction of the magnetic flux penetrating the solar photosphere occurs in elements with field strengths in excess of 1 kG. The elements range in size from large sunspots with diameters exceeding 20 Mm, down to tiny flux tubes whose diameters are inferred to be smaller than 100 km. The occurrence of strong fields in discrete structures of this kind has important consequences for our ideas concerning the generation, evolution and decay of solar magnetic fields, the structuring of the solar photosphere, chromosphere and corona, and the origins of non-radiative heating and mass transfer in the solar atmosphere. The observed properties and theoretical consequences of highly structured, intense solar magnetic fields were discussed at a recent meeting held at Sacramento Peak Observatory (SPO).*

J. Harvey (Kitt Peak National Observatory), summarised the current observational picture of small scale magnetic fields. Magnetograph observations of the net flux in areas greater than about $(2 \text{ arc s})^2$ show that in the quiet Sun almost all flux is concentrated in 1-2 kG 'bundles,' which occupy only a small part of the observed area. The area occupied by the strong field increases with increasing height, as the field flares out. In the general neighbourhood of the area where the flux elements penetrate the photosphere, there is a perturbation in the photospheric brightness distribution (called filigree or facular elements) and in the absorption line spectrum (line gaps); however, there is not a one-to-one spatial correspondence between the magnetic and brightness structures. This implies that there is not a tight temporal correlation between the evolution of brightness structures, which change in a few minutes and magnetic structures, whose evolution has not yet been studied with adequate spatial resolution.

The correlation between magnetic and velocity fields in the flux bundles is a perplexing problem. Many observers have found that the material in the magnetic

elements is flowing downwards with a velocity of the order of 1 km s^{-1} . In a careful study, Giovanelli and Slaughter (*Solar Phys.* 57, 225; 1978) showed that there is a downdraft whose amplitude increases with depth, highlighting the following problem: if the conductivity of the solar atmosphere is as high as is universally assumed, the field lines should be frozen into the plasma. If this is the case, whence comes the large mass flux that is continually flowing down the magnetic elements? Avoiding the problem of the origin of the downdrafts, E. Parker (University of Chicago) showed how the magnetic elements could be cooled, and thereby maintained in concentrated form, by such flows.

During periods of good seeing, the extremely sensitive Kitt Peak magnetograph reveals small-scale bipolar structures almost everywhere on the solar surface. These are distinct from the small-scale intense flux tubes that occur predominantly in the photospheric network, and are called the inner network field (INF). The properties of the INF are not well known. As A. Title (Lockheed) reported, a magnetogram obtained at SPO with 0.5 arc s spatial resolution does not reveal an INF component with a rms field strength exceeding 50 G. The possible existence of a chaotic magnetic field with a strength of a few gauss, pervading the entire solar photosphere, has great theoretical implications, and the demanding observational problems of high sensitivity and superb spatial resolution will be attacked by observers in an effort to tie down the properties of the INF.

Parker stressed the vital importance of solar studies as the foundation for astrophysics. "If we don't understand the relatively well-observed MHD phenomenon of sunspots, how can we have confidence in speculations about MHD and plasma processes in such objects as quasars and galaxies?" he asked. Parker described the physical basis of several characteristic properties of small-scale intense magnetic flux tubes, and highlighted some of the basic theoretical problems posed by the existence of small-scale magnetic structures and sunspots. His recent sunspot model (*Astrophys. J.* 230, 905; 1979) was discussed, but the general consensus among observers and theoreticians alike was that the formation, evolution and decay of sunspots are, in most respects, unsolved problems.

N. Weiss (University of Cambridge) discussed the connection between surface magnetic fields and the magneto-gas dynamics of the solar interior. He emphasised the importance of flux emergence in ephemeral active regions (EAR, closely related to X-ray bright points). When these are taken into account, the rate of flux emergence through the solar photosphere is essentially constant through the solar cycle (about $3 \times 10^{22} \text{ Mx per day}$), and is sufficient to

replace the surface flux every 10 days. This fact, together with the fundamental property of solar magnetic fields to appear always in the form of strong-field flux tubes, poses tremendous problems for the theory of the cyclic generation, transport and reversal of solar magnetic fields by dynamo action.

The most advanced existing dynamo models are based on mean-field electrodynamics, but the existence of intense, inhomogeneous solar surface fields strongly suggests that mean field theory is inappropriate. Weiss suggested that a more realistic picture of the solar interior would involve a constantly changing framework of magnetic structures with convective eddies lying between them. Any description of dynamo action in such an intermittent magneto-convective region would involve a 'flux-tube dynamo.' Weiss sketched a model of this kind, involving field generation in a zone of penetrative convection between the solar radiative core and convective envelope. Such a model has the advantage of providing a relatively ordered field by avoiding the inevitable 'tangling' by convection acting over a time scale of years, and it also removes one of the major problems of flux-rope theories, that magnetic buoyancy in the convection zone forces flux to the surface too rapidly.

It is interesting to note how the changing observational picture of solar magnetic fields has vindicated many of the objections to conventional theories made by J. Piddington (CSIRO: see *Astrophys. Space Sci.* 55, 401; 1978). Piddington has been frequently criticised for not providing a 'rigorous mathematical treatment' to support his ideas, but as he pointed out, "no treatment is acceptable, let alone rigorous, unless it is based first on adequate observational data and second on sound physical interpretation." Probably our understanding of solar magnetic fields will improve with the melding of Piddington's picturesque models with the powerful mathematical methods being developed to study intermittent MHD turbulence.

In summarising a number of important observational problems that emerged from the meeting, C. Zwaan (Utrecht) emphasised the need to study in detail the physical processes occurring in single small flux tubes. Such studies require sensitive velocity and magnetic field measurements to be made over relatively long periods with excellent spatial resolution. The 1.25 m Shuttle Optical Telescope (SOT) designed by R. Dunn (SPO) will provide the technological leap required to answer problems concerning solar atmospheric structures on the 100 km scale. Other important problems may not need such new instrumentation, but rather the careful application of existing equipment. One fascinating question is 'how does

Lawrence E. Cram is Staff Astronomer at Sacramento Peak Observatory, Sunspot, New Mexico.

*A summer symposium on Small-Scale Solar Magnetic Fields was held at Sacramento Peak Observatory on 16-21 July, 1979.

magnetic flux disappear from the solar photosphere?"

There is a growing body of evidence pointing to the widespread existence of stellar chromospheres, coronas, and winds, all of which seem to be variable and many of which may be related to

'magneto-gas-dynamic processes' in stellar atmospheres. A sobering conclusion of the meeting was that we must do much more work to understand the intricacies of solar magnetic fields, and it will be a long time before a satisfactory account of stellar and cosmic electrodynamics is available.

Rapid screening of carcinogens — end of the beginning?

from Philip D. Lawley

THE problem of the aetiology of cancer is now of no mere academic interest, but of considerable socioeconomic importance, in the face of increasing public scepticism regarding effective prevention or treatment.

Recent recognition of the importance of rapid screening for potential carcinogens (almost synonymous with testing for potential mutagens according to methods devised by B.N. Ames) followed from the hope that elimination of these chemicals from the environment would lead to a significant reduction in cancer incidence. However, this optimism seems to be drifting away, as, for example, estimates of the occupational component of cancer incidence first increased, from their generally accepted lowish level (1-5%), to a forecast of 23-38%, followed by a reaction against the higher figures.

This sense of scepticism is not confined to epidemiologists and cancer aetiologists. If informed current opinion is represented by such a respected literary figure as Susan Sontag (in her recent book, *'Illness as Metaphor'*), then both historically predominant themes in cancer aetiology, the 'environmental-mutagenic-chemical' and the 'hormonal-developmental-immunological', are dismissed, and the cause of cancer is maintained as an unsolved mystery. (These themes can be traced back, for the latter school of thought, to observations on proneness to breast cancer of 'melancholic' as opposed to 'sanguine' women by Galen (2nd century AD), or of nuns (Ramazzini, 1700); or, for the environmental school, to those on chimney-sweeps' cancer by Pott (1771)).

The more recent 'somatic mutation' theory originated a mere hundred years ago, and found biochemical support from observations that the alkylating agent, mustard gas, later established as a carcinogen in man, reacted with nucleic acids *in vivo*, a finding subsequently extended to virtually all classes of chemical carcinogen.

The invaluable 'Ames test' (in reality a mini-battery of tests using bacteria as the test organisms) permits rapid bioassay of

chemicals, or their reactive *in vitro* metabolites, for mutagenic activity. However, to validate this test against many known carcinogens (established through conventional animal tests), it has been necessary to strip the bacteria of their DNA repair capability, and to sensitise them further by introduction of a mutator plasmid. The *in vitro* metabolic activation system (from liver of rats) rarely, if ever, mimics exactly the metabolism of carcinogens *in vivo*, even in rat liver, itself rarely the target tissue.

Furthermore, a fundamental difference exists between the DNA repair capability of bacteria and that of mammalian cells, which has been recognised from the earliest comparative work. Mammalian cells can reproduce apparently quite normally, as judged by survival of colony-forming ability and lack of induced mutation, despite incomplete removal of chemically (or radiation) induced DNA damage. Whether this indicates more effective repair (the remaining damaged DNA being redundant), or whether it is a source of further potential mutations, perhaps remains debatable. Nevertheless, mammalian cells, and in particular normal human fibroblasts, are remarkably resistant to low doses of mutagens or carcinogens, by these criteria.

The overall picture to the biochemist is, therefore, that any quantitative correlation between rapid screening data and the risk of human cancer from exposure to the test chemical is likely to be tenuous, *a priori*. Against this background, and with the now prodigious interest in, and expenditure on (at least in the US), this area of research, it was indeed appropriate that a conference* should be called to undertake a rigorous examination of this relationship. In addition, the associated fledgling topics of possible rapid screening methods for teratogens and nephro and neurotoxic chemicals were discussed, in the light of experience with the parent 'Ames tests'.

The topics covered in this blockbuster of a conference ranged from 'Molecular Mechanisms of Carcinogenesis' to 'Risk Assessment Approaches for Establishment of Criteria and Standards', culminating in a round-table discussion on 'Development of Environmental Policies', this last dominated by the eloquence of a named US Presidential candidate, B. Commoner (Washington University, St Louis).

On molecular mechanisms, the emphasis is shifting to recognition that while the initiation stage (somatic mutation) may be necessary for carcinogenesis, it is not of itself sufficient. Subsequent stages (denoted by some as 'promotion', somewhat to the dismay of P. Shubik (University of Heidelberg, an originator of the concept) may be at least as important, and there was much talk of 'synergism', 'cocarcinogenesis', and 'late stage carcinogens'. M. Radman (Université Libre de Bruxelles) thought that X-radiation had more of the characteristics of a promoter than of an initiator, and that promotion involved chromosomal rearrangement, but other speakers stressed the involvement of the interaction of promoters with cell membranes. Shubik questioned the tendency of some to attribute reversibility to the process of promotion.

With regard to the fundamental and over-ridingly important question of relevance of rapid-screening to the assessment of human cancer risk, I cannot do justice here to the thorough discussion of the topic that was given. As a UK taxpayer one remains uncertain whether shame at one's country's lack of expenditure on toxicology, or admiration of the US research effort in this area, should be the predominant emotion.

M. Waters (EPA, Research Triangle Park) showed convincing evidence from tests at various levels, and from epidemiological studies, particularly for a range of pesticides, that 'tier tests' were not an acceptable vehicle for assessment of cancer risk, and that a 'battery' of tests, including conventional animal life-time carcinogenesis studies, was notably less fallible. He held out some hope for a test based on transformation of human cells in culture, but the notorious difficulties already encountered seem to be in line with the known relative lack of susceptibility of normal human cells to carcinogens.

This indication also emerged from the thorough comparative assessments (by R. E. Albert (New York University) and others) of the results of quantitative animal carcinogenesis tests and human epidemiological studies, using the conservative assumption of linear dose-response at the low doses of environmental chemicals to which man is exposed. Generally man emerged as, at most, rather less susceptible to environmental carcinogens than the animals used in the conventional tests. From the reasonable estimates of the levels of environmental exposure, it seemed unlikely that these could account for a substantial proportion of the aetiology of human cancer. The current trend was expressed as 'downgrading of environmental causality'.

Another controversial issue concerned

P.D. Lawley is at Pollards Wood Research Station, Institute of Cancer Research, Chalfont St Giles, Bucks, UK.

*Nato Advanced Research Institute, Monaco, 22-28 September, 1979: *In vitro Toxicity Testing of Environmental Agents: Current and Future Possibilities*, organised by A. Kolber (Chairman) (Research Triangle Institute, North Carolina), L. Grant (US Environmental Protection Agency), S. Harry (US National Institute of Environmental Health Science) and J. McLachlan (USNIEHS) and T. Wong (Research Triangle Institute).

the implications of results from rapid screening for regulatory policy. Previously (see *Nature* 278, 388; 1979), President Carter's advisers at the US Office of Science and Technology expressed the view that "it is necessary to start by distinguishing scientific from regulatory decisions" — "scientific data collection and analysis" was one matter, but "cost benefit analysis" definitely another.

This view did not seem to be shared by B. Commoner, who began his presentation of results, from Ames tests of human body fluids and foodstuffs, by stating his belief that this type of experimental work could, in certain cases, supersede epidemiological studies, and did have direct implications for regulatory policy.

On the lighter side, he included an entertaining account of his work showing that red onions contain mutagenic flavonoids, leaving white onions, in the absence of any known specific nutritive value of their congeners, as winners in the risk-benefit analysis.

Some asperity developed between Commoner and R. Morgan (University of Toronto), who expressed the anguish of at least some of his fellow epidemiologists, that "the Ames test has led to more hypotheses than could possibly be tested", but, perhaps in some compensation, has been of distinct benefit to the legal profession. In an elegant presentation, Morgan showed that, in agreement with epidemiological experience, increasing the sensitivity of a screening test (certainly a marked feature of the history of Ames' tests) necessarily decreases its specificity and hence its predictive value.

The 'book of the meeting' will be required reading for many administrators (or indeed any of the public seeking a comprehensive view of this important area of research) as well as cancer aetiologists and toxicologists in general. □

The fascination of echinoderms

from Norman Millott

ECHINODERMS do things differently, which is one good reason why they have attracted increasing numbers of biologists with widely differing specialisations. This appeared to advantage in a recent colloquium*. Communications were so many and varied that only a few of the many excellent ones can be mentioned here.

Palaeontologists — seemingly tireless in their devotion to the group — were in part concerned with rare fragments of Jurassic

echinoids from Western Australia indicating a wide and rapid spread of cassiduloids. Others challenged existing ideas concerning the primitiveness of the cidaroid lantern, or urged the need for a critical revision of classical changes in Adriatic echinoids to deepening of the sea, changes in climate and sediment and accumulation of calcium carbonate. D.G. Stephenson (Keele University) advanced yet one more idea concerning the seemingly eternal mystery of the five-rayed symmetry, showing that it could have conferred advantages in passive suspension feeding and could have been independently evolved in various groups of echinoderms.

Taxonomy, ever restless, was represented in the findings concerning holothurians of a 28-year survey of the Chinese coast, yielding incidentally, two new species and a proposed new genus. Other communications argued for regarding *Holothuria stellata* as a genuine species and for transferring the genus *Ophiocoma* to the Ophiacanthidae.

Ideas concerning the affinities and phylogeny of echinoderms invariably command attention. H. and G. Termier (Université P. et M. Curie, Paris) envisaged the evolution of coelomates as involving an early separation of echinoderms from lophophorates and chordates, with development of 'architectural' diversity and adaptive radiation in the Cambrian. R.P.S. Jefferies (British Museum (Natural History)) also painted a broad canvas, adding more detail to his picture of chordate evolution, deriving these animals from his palaeozoic Calcichordates, which show echinoderm affinities, yet possess what he interprets as tell-tale characters of chordates.

Echinoderms have nothing if not spectacular coelomic systems, achieving much by hydrostatic pressure, circulation of coelomic fluid and wandering cells. J. Binyon (Royal Holloway College, University of London) reported experiments determining the level to which fluid pressure could be raised in starfish before structural damage occurs, while C.W. Walker (University of New Hampshire) supported by direct observation, the importance of flagellated collar cells in producing coelomic circulation. Some functions of the ubiquitous wandering cells, including their bactericidal action, were elegantly demonstrated by L.I. Messer and A.C. Wardlaw (University of Glasgow) and a very different relationship with bacteria in *Leptosynapta* was reported by J-P. Feral (Muséum National d'Histoire Naturelle, Paris) who described their constant association with cuticular structures. Others demonstrated the ultrastructure and symbiotic associations of amoebocytes, their relation to lesions in the body wall and their importance in transporting gut enzymes. The importance of the enigmatic 'haemal' system in moving

assimilated substances, accumulating lipids and eliminating effete phagocytes was also indicated.

The extraordinary plasticity of peritoneal cells which Farmanfarmanian and I showed in 1967, received striking confirmation from A. Van Der Plas and M. Jangoux (Rijksuniversiteit, Utrecht & Université Libre de Bruxelles) who described the migration of these cells into the epithelial lining of the pyloric caeca of *Asterias* to form lipid stores showing changes related to the reproductive cycle.

Concerning the nervous system, there were reports of an unusual mode of dual innervation in echinoid podial muscles, of the importance of the radial nerve and its own sector of the nerve ring in the arm regeneration of *Asterina* and (for a change!) an analysis of associative learning in *Marthasterias*.

Physiological flexibility was the keynote of communications concerning rock pool species and the remarkable tolerance of sudden and extensive salinity changes of *Ophiura albida* in Loch Etive.

Much was said about nutrition, including the partition of energy between respiration, excretion and growth in plutei, and in starfish, changes in diet and population structure which occur with depth were reported, as well as the existence of a 'waiting stage' between larval and growing phases when food is scarce. Differing feeding processes in echinoids were correlated with differing fine structure of their radiole spines, and it was indicated that the shallow water holothurians of Enewetok Atoll do not occupy the same habitat unless they have different feeding habits.

Population dynamics with undertones of pollution and economics were represented in separate accounts of the effects of sewage sludge dumping near the mouth of the Elbe, where brittle stars were involved in the ensuing instability of the benthos, and of the possibility of introducing threatened edible species into suitable sites. Impressive densities of echinoderms off the west coast of Ireland and their dominant role in benthic economy were emphasised by a group of workers from University College, Galway. These were the contributions of professional scientists, but D. Nichols (University of Exeter) rightly paid tribute to the important contributions to his survey of threatened *Echinus*, made by amateur and professional divers.

As befits a modern programme, biochemistry and cytochemistry were represented by reports concerning the importance of steroids and the occurrence of gut enzymes in various species as well as the different aspects of the action of 1-methyladenine on starfish oocytes in which a calcium-binding factor resembling calmodulin was reported. □

Emeritus Professor N. Millott is at the University Marine Biological Station, Millport, Scotland.

*A European Colloquium on Echinoderms, dedicated to L. Cuénot, was held at the Université Libre de Bruxelles on 3-8 September. It was organised by Dr. M. Jangoux, Laboratoire de Zoologie.

AUTUMN BOOKS

IT is widely known that Enrico Fermi and his team started the first controlled nuclear chain reaction on December 2, 1942, in Chicago. This book tells us how a Frenchman, Frédéric Joliot, rather than Fermi, might have become the Prometheus of the atomic age, but for the German occupation of France. Madame Curie had picked the promising youngster for her assistant in 1925; she soon saw that he was a "skyrocket". Two years later he married her daughter Irene, the chemist, and thus entered the scientific circle, in the highly stratified society of Paris. Some saw him as a gate-crasher; and he always felt happiest with workers or fishermen.

His research at first brought him some disappointments. In 1931 he published observations which led James Chadwick to the discovery of the neutron and to the Nobel Prize; the next year he narrowly missed the discovery of the positron. But then at last came success: early in 1934 he and his wife published their observation of "artificial radioactivity". That important discovery brought them jointly the 1935 Nobel prize for chemistry and secured for Joliot the first Chair for Nuclear Chemistry, at the Collège de France.

In January 1939 Otto Hahn and Fritz Strassmann published their famous paper which indicated the fission of uranium nuclei struck by neutrons; Irène Joliot-Curie, who had narrowly missed that discovery, "bitterly regretted that she and her husband had not worked together on the problem, for their combined brains might well have solved it". At this point, about a quarter through the book, begins the main story.

Within a few days, Joliot had seen the stupendous implications of that new

phenomenon: the possibility of a nuclear chain reaction which could release energy on a large scale. Leo Szilard had been looking for such a reaction since 1934, and Joliot had said in a public lecture in 1935 that "compared with the neutron, the philosophers' stone of the alchemists was a childish fantasy; doubtless people would soon be able to change lead into gold, but this would be an insignificant by-product compared with the enormous quantity of energy that would be released". Now, he

Prometheus of the atomic age

Otto R. Frisch

Scientists in Power. By S.R. Weart. Pp.343. (Harvard University Press: Cambridge, Massachusetts, and London, 1979.) \$17.50; £11.35.

felt, it was up to him to create that chain reaction which would present almost unlimited energy to France and hence to the world.

First of all he had to make sure that the fission of uranium nuclei released neutrons, as expected. Hans von Halban, son of an Austrian-born professor, was in Paris and keen to join Joliot in tackling that tricky problem, having gained experience with neutrons in Copenhagen (jointly with the reviewer). He in turn recruited Joliot's "little typist", a huge Russian called Lew Kowarski who was determined to become a scientist and did secretarial work to get a foot in the door and to supplement his meagre income from design work in a factory of gas pipes. Trained as a chemical engineer (see my obituary notice of Kowarski in *Nature*) he brought a valuable new way of thinking into the team. Those were the three musketeers who soon agreed that in publishing their joint work they would always share the credit for all ideas, whoever had thought them up.

By the end of February they knew that a chain reaction was not impossible: uranium produced more fresh neutrons than it swallowed. But were there enough of them? Some would escape from the material or be absorbed by its impurities. The team had to know the average number of neutrons released when a single uranium nucleus suffered fission, and by the end of

April they thought that number was about 3.5. Today we know that the number is nearer 2.5, but perhaps the error was to the good; it made a chain reaction look easy to achieve and thus encouraged the team to redouble their efforts.

From the beginning they had studied uranium salts dissolved in water, in a tank about 1 m in diameter, with a neutron source at the centre. The neutron distribution in the tank was measured by placing small foils of dysprosium at various distances from the source and, after a standard time, measuring their radioactivity with a Geiger counter; that gave information on the number and the average speed of the neutrons. The water prevented most neutrons from leaving the tank and thus escaping scrutiny; it also served as a 'moderator' which slowed down the neutrons and made them more effective in causing fission. Promising as the results were they came nowhere near a self-sustaining reaction; it was soon clear that much more uranium would be needed.

In May 1939 Joliot approached the Union Minière du Haut-Katanga, a Belgian copper-mining firm which, almost as a sideline, extracted radium from its uranium ore. They had plenty of surplus uranium, and Joliot got them to ship five tons of pure uranium oxide to his Laboratory for Nuclear Synthesis at Ivry (near Paris), with its huge hangar and heavy handling equipment. In July Halban began the tedious neutron density measurements on spherical metal containers filled with a black mud, a mixture of uranium oxide and water, up to three atoms of hydrogen to one of uranium; the oxide would not soak up more water. When War broke out in September they had tested

Sorry, for copyright reasons some images on this page may not be available online

Sorry, for copyright reasons some images on this page may not be available online

Sorry, for copyright
reasons some images
on this page may not
be available online

spheres up to half a metre in diameter and had clear evidence of a chain reaction that roughly doubled the number of neutrons that came from the source; but it was still far from self-sustaining. Water was not a good moderator; too many neutrons failed to cause fission because they were captured by its protons.

But what other moderator could one use? Carbon, as graphite, was available by the ton, but with its nuclei twelve times heavier than protons, neutrons needed many more collisions to become slow. Would they survive so many collisions without being captured? Much time was lost experimenting with piles of solid carbon dioxide ('dry ice') and industrial graphite; the results were promising but not conclusive. In the USA, similar work was done later and more carefully, convincing Fermi that graphite could be used; about the same time, a wrong result caused the Germans to abandon graphite as a moderator.

In the meantime Kowarski urged his team to consider heavy water: instead of protons it contains deuterons, only twice their mass, and it hardly absorbs neutrons. But it has to be extracted, at great cost, from ordinary water, of which it forms a minute fraction; in the USA, available only by the tumbler, its use was quickly dismissed. But in Europe the Norwegian firm Norsk Hydro had made almost 200 litres and were ready to increase production. In February, lieutenant Jacques Allier, a former employee of the French bank that controlled Norsk Hydro, went to Norway and persuaded them to hand over their whole stock, free of charge. The Germans were expected to interfere by force, and the entire operation reads like a spy thriller. Until the heavy water arrived in Paris in the middle of March, those two dubious foreigners, Halban and Kowarski, were interned for three weeks on two separate islands!

But in May the German army invaded France. After a brief attempt to set up a new laboratory in Clermont-Ferrand, Joliot decided that the team must split up; he would remain in France while Halban and Kowarski were to resume the work abroad. On June 17 they drove west in their cars, with their families, laboratory notes and the heavy water; in Bordeaux they embarked on a British collier which safely got them to London on June 22, just as

France signed an armistice.

The British installed the team and gave them help at the Cavendish Laboratory, Cambridge. An aluminium sphere was constructed and filled with mixtures of uranium oxide and heavy water; it was made to rotate slowly to prevent the oxide settling to the bottom. After five months they had good evidence that a still larger sphere would give a self-sustaining reaction. But Fermi was still sceptical. Moreover, the USA were suspicious of Halban who stressed the French patents and got help from ICI (Imperial Chemical Industries); why help those probable post-war competitors? Negotiations dragged on for nearly three years.

To remove the work from this beleaguered island, a transfer to Canada was prepared; but when it at last took place late in 1942 — just as Fermi won the race for the chain reaction — some of the Cambridge physicists decided to stay with Kowarski, who had refused the inferior position Halban had offered him in Canada. Both teams had to live through another year of slow progress and low morale.

The Quebec Meeting of Churchill and Roosevelt finally enabled Canada to get information and heavy water from the USA. Replacing Halban, (Sir) John Cockcroft took charge of the Canadian team which was now joined by the Cambridge scientists. It took Kowarski less than a year to build a heavy-water reactor,

Sorry, for copyright
reasons some images
on this page may not
be available online

which began to operate — the first outside the USA — a month after the War came to an end.

Joliot led a double life during the occupation. He kept his Paris laboratory going, but subtly sabotaged any research which Germany tried to conduct there; and he worked in the Resistance and came to admire the communists for their courage, idealism and competence. When France was liberated he was tireless in reviving fission research, amidst political strife and a ruined economy. Equipment was requisitioned or home-made; young people, attracted by the glamour of nuclear energy, were trained. Before Christmas 1948 the first reactor in France began to operate a heavy-water reactor, again built by Kowarski.

After that, the power of the scientists began to decline as the engineers, administrators and politicians took over. The declaration that France would never build nuclear weapons was gradually forgotten. Joliot's communist stance caused increasing problems, and after a rally in April 1950 when he declared that France would never make war on the Soviet Union he was removed from his post as head of the Commissariat à l'Énergie Atomique. Large reactors were built, optimised for the production of plutonium, and the first French Bomb was exploded over the Sahara in 1960.

Joliot is clearly the hero of the book, a scientist who combined hard logic with lively imagination, and a persuasive personality with considerable skill as organiser. In his bid for nuclear power he was up against Fermi, probably the greatest all-round physicist of our time, as experimenter and theoretician alike, while France was short on theory. But Fermi was cautious and a foreigner in the USA while Joliot was full of fire and had the support of his country and his government. The author quotes Lord Blackett for saying "had the war not intervened, the world's first self-sustaining reaction would have been achieved in France".

This is a very well researched book, with its 12 pages of bibliography, 35 of footnotes, and a good index. But in spite of that scholarship the book is eminently readable and contains deft pen portraits of its many characters. It is written with a quiet dignity that yet does justice to the dramatic events with which it deals. Spencer Weart focusses on the French story but gives fair attention to efforts made elsewhere. Scientific explanations are kept fairly brief; much more space is given to the delicate interplay of social, economic and political forces; of great families and great schools; of scientists and administrators. Whichever way you look at it, this is a valuable and fascinating book. □

Otto R. Frisch was Professor Emeritus at Trinity College, Cambridge, UK. In Copenhagen he had contributed to the discovery of nuclear fission early in 1939. Professor Frisch died on 22 September, 1979.

Curiosity of a scientist

Hermann Bondi

Disturbing the Universe. By Freeman Dyson. Pp. 283. (Harper and Row: New York and London, 1979.) \$12.95; £6.50.

OCCASIONALLY I feel unkind towards my many friends and colleagues in the education industry by pointing out that every small child makes a nuisance of itself by constantly asking "Why?", that society has developed a marvellous defence mechanism called education, and that this is so effective that it stops almost everyone from keeping on with this questioning. The few failures of this cure are, I claim, called scientists.

Curiosity must indeed be the mainspring of scientific endeavour. The constant nagging feeling of *wanting* to know something or other that is well hidden is indeed a powerful drive. To find out what a particular problem really is like and has as its solution, to worry the problem like a dog worries a bone, to gain insight by following to their end innumerable false turns, to see the whole confusing jumble eventually form a surprising and unexplored pattern, that is the real compulsive urge and joy of a scientist's labours.

To an extent that varies markedly between individuals there is associated with this an urge to communicate, an urge to teach, an urge to show to others the lovely pattern one has seen (whether one has found them or made them is a moot point) in one's own sandbox. Thus, research and teaching are naturally linked, but the link may take many different forms. To interest suitably qualified colleagues or research students in one's own researches is natural enough, but to watch a research student learn by making his own mistakes, perhaps messing up a lovely corner of one's sandbox is more of an acquired taste needing much self-discipline, but with its own rich satisfaction when one's pupil finally soars off under his own power. Undergraduate teaching is often seen as a chore, but only by those who have not got the urge to get across the beauty one sees in the structure of one's subject, the pleasure of conveying the personal pattern that one has seen (or made) in a well known part of the field.

Thus, there is substance to the notion of the normal academic career where one's researches (the value of which can be judged reasonably well) lead to posts in which teaching (the quality of which it is much harder for a university to assess) forms a major part of one's duties, along with continuation of one's research.

However, justification for the curious habit of academic tenure (other than the mental comfort of the holder) can surely only be found if it enables the incumbent to follow daringly different unconventional and potentially fruitful pursuits on which he would otherwise not have embarked. Unhappily it is only a minute minority who so use their freedom. The vast majority of tenured academics, even of full professors who have nowhere further to rise, turn their academic positions or chairs, not so much into comfortable beds, as into narrow grooves of dried-up specialism often made most uncomfortable by making an 80 hour week out of administrative tasks that would take a competent bureaucrat half of an afternoon. Rare indeed is the person who really uses the freedom given by academic tenure to enrich the world and to enjoy himself by working hard and effectively at each in turn of the wide variety of pursuits he finds intriguing. Pre-eminently one such is Freeman Dyson, and his book is an exciting journey through the broad landscape of his experiences and thoughts.

Perhaps this is the point at which I should interpose the story of my period of friendship with the author which illustrates some of the bits he so oddly left out of the book. He does not mention his extraordinary brilliance at school at Winchester and as undergraduate at Trinity College, Cambridge, in the bumper class that had in it James Lighthill and Freeman Dyson, a record pair not equalled before or since. After the painful interlude of Bomber Command (fully described in the volume) he returned to Trinity as a young Fellow a few years my junior. An inveterate talker like myself (I recall his interrupting me at High Table dinner with "Not another word now. We are still on the soup while the other are finishing their desserts") he clearly had a most enjoyable year, but found that Cambridge, with its then rigid barrier between Physics and Mathematics was not a good place to learn and work in the lively field of theoretical quantum physics he wished to pursue. Hence his move to Cornell and Hans Bethe, where his book restarts. Why this odd omission of Cambridge?

He relates how he learned, travelled, and did brilliantly, none of which surprised me. But I was astonished and a little worried when he accepted a permanent position at the Institute of Advanced Studies in Princeton. That such an able and enterprising young man should take a post from which there was no escape upwards in academic life, a post that would hang round his neck for nearly 40 years, that would prevent him from teaching anyone but a few highly selected graduate students, that would isolate him in a closed esoteric community, all this saddened me greatly. How wrong I was to worry is so beautifully shown in his book. To him the Institute post was simply a springboard for pursuing

his foibles, and for one such as Dyson each foible is both what would be the adventure of a lifetime for others and a notable contribution to mankind's storehouse of knowledge and experience.

Two of his particular characteristics are to be totally fascinated by space, and to be deeply interested in nuclear power. He describes with such evident joy his cooperation with a brilliant group of people to design the 'inherently safe' Triga nuclear research reactor. In very little time the endeavour was most successful, and dozens of these reactors were sold. Not long afterwards Dyson was involved with the splendidly conceived Orion project which aimed to use nuclear power to make space travel cheap and fast. In the end, this

mankind's future in space as he sees it. I happen to be more of a doubter in this field, but I too was carried along by the sweep and logic of his vision, by his imaginative application of knowledge, by his sheer enthusiasm. I tend to think that the solution of our problems on the Earth must be found on the Earth, but his comparison with older efforts of settling new lands is certainly intriguing and well argued, his view of the need for adventure is stimulating, and the whole section is not just very readable, but truly exciting and thought provoking.

I am less enthusiastic about the pieces of Dyson's personal history in the book. They certainly are well chosen fragments, but they are only fragments. One's personal

Sorry, for copyright reasons some images on this page may not be available online

endeavour was doomed through external developments. He describes his involvement with molecular biology more sketchily but the depth of his understanding is evident. Politics fascinated him, not the strident shouting of electioneering that is so liable to expand minor differences of judgment on non-central issues into great philosophical divisions, but the patient work of exploring how the most deeply held and widely differing convictions can be reconciled in modest and valuable programmes of action. His work in the Arms Control and Disarmament Agency and his efforts in the Princeton Citizen's Committee to advise on whether recombinant DNA researches should be permitted are all lovingly related in a most human and readable manner. Much earlier, in the Oppenheimer tragedy, he seems to have been only a spectator, naturally an immensely concerned spectator, but one with much understanding of how some actors came to what he regards as utterly wrong choices. This was his bleeding in politics, and if it left him wounded, he was keen to point out the total absence of scars.

But perhaps the most thrilling part of the book deals with his deep speculations on

life is a continuous chain of experiences and impressions, each section being properly intelligible only in the light of its predecessors. His episodes, though, make excellent reading matter. He is also curiously reticent about his scientific work since his appointment to the Institute.

But to come back to the mainstream of his book, I was especially intrigued by his fascination with engineering, a fascination I, as another theoretical physicist, share with him, though he came to it earlier in life than I did. But where he and I differ is in our attitudes to bureaucracy. It is natural for a scientist to feel antipathetic to big organisations. The brilliant ideas, the outstanding contributions we most admire and indeed venerate, are necessarily the product of one person's mind, or very occasionally of two or three closely collaborating minds. Ten thousand mediocrities working for ten thousand years could not have duplicated Einstein's ideas or those of Charles Darwin. Exceptional quality of mind is needed in our fields and cannot be replaced by quantity. But great engineering projects like Apollo, or the Forth Bridge, or Concorde, are created, and can only be created, by vast impersonal organisations responding only slowly and gently to any

ELLIS HORWOOD

Publishers Chichester



CELL POPULATIONS

Editor: **E. Reid**, Director, Wolfson Bioanalytical Centre, University of Surrey

This desk guide to new and established methods of isolating cell populations from tissues or other heterogeneous biological sources surveys techniques for obtaining homogeneous samples of healthy cells from mammalian tissues, and from protozoan and other free-living cells. It also offers guidance on the choice of the most suitable methods. The range of techniques covered includes sedimentation, isopycnic banding, elutriation, partition between two aqueous phases, and free-flow electrophoresis. It will serve as a research and laboratory reference book, or as a teaching aid, providing also adequate background knowledge for non-specialists. It is an authoritative coverage of the field by an international team of experts, first presented at a Subcellular Methodology Forum held at the University of Surrey in 1978. There is no such wide-ranging survey of its size known to be available.

Contributors include: W.S. Bont, N. Crawford, M.J. Crumpton, W.H. Evans, R.J. Hay, H.G. Heidrich, G. Johansson, D.L. Knook, H.A. Krebs, S.M. Lanham, J.P. Luzio, H. Pertoft, G. Raydt, I. Schulz, P.O. Seglen, and Th. J.C. van Berkel.

Series: *Methodological Surveys (Series B: Biochemistry)* Vol. 8

October 1979
085312 120 6

252 pages
\$45.15/£18.50

PLANT ORGANELLES

Editor: **E. Reid**, Director, Wolfson Bioanalytical Centre, University of Surrey

This comprehensive and critical survey of known methods of the isolation of organelles and membrane material from plant tissue also emphasizes the advances in the field.

The book first considers methods for isolating bioenergetic organelles, and then presents current views on vacuoles and microbodies. There is consideration of membranous components and nuclei, and of constituents such as glucan synthetases and phytochrome, with attention to lectins, auxin binding and glycosyl transferases. The critical collation of current thinking on markers for characterizing subcellular fractions concludes this outcome of a Subcellular Methodology Forum held at the University of Surrey in 1978.

Contributors include: H. Beevers, D. J. Bowles, R. Douce, J. L. Hall, R. Hertel, C. Larsson, R. A. Leigh, J. M. Lord, G. MacLachlan, A. E. C. MacRobbie, D. Marmé, D. J. Morré, C. A. Price, P. H. Quail, P. M. Ray, S. P. Robinson and E. L. Vigil.

Series: *Methodological Surveys (Series B: Biochemistry)* Vol. 9

October 1979
085312 123 0

242 pages
\$45.15/£18.50

Distributed by
John Wiley & Sons Limited

Baffins Lane, Chichester, Sussex, England

Circle No. 54 on Reader Enquiry Card.

change in direction, whether the command comes from a genius or from a mediocrity. They can be accelerated slightly by leaders of great drive, and lose momentum without leadership. But invariably they grind on remorselessly, very inefficiently, but necessarily successfully, for only mass murder could stop them in their tracks.

It needs a certain type of sophistication to derive job satisfaction from the awareness that, without one's sustained efforts over a year, the organisation would be moving in a slightly different direction, and would not have got quite so far. Such a form of sophistication Dyson does not have. To him only work in a small group is

fun. This attitude separates him from much modern engineering and from much that is involved in the public service. He is thus a supporter of small bands of pioneers rather than of large project management teams. It is a great loss that our necessarily large bureaucracies are unable to attract such talent.

I am sure I have said enough to make it clear that I thoroughly enjoyed reading this book, that it gave me a lot to think about, and that I can recommend it heartily to all. □

Sir Hermann Bondi is Chief Scientist at Her Majesty's Government's Department of Energy.

A man who thinks otherwise

Eric Ashby

The Medusa and the Snail: More Notes of a Biology Watcher. By Lewis Thomas. Pp. 175. (Viking: New York, 1979.) \$8.95. (A UK edition will be published after May next year by Allen Lane (London).)

IN far off days, when the academic profession was a revered élite, the Germans defined a professor as "a man who thinks otherwise". In these days, when knowledge is fragmented and the academic profession unionised, otherwise-thinking is rare, even among professors. Hence the significance of this little book of essays, for Lewis Thomas is a virtuoso in thinking otherwise.

At first glance the book seems to be lightweight, no more than a capricious assortment of fancies about ponds in Manhattan, cloning of human beings, committees, punctuation, disease, death, warts; all gently mischievous, witty, conversational in style, the work of a latter day Montaigne or Lamb. Those who have read Thomas' other essays (*The Lives of a Cell: Notes of a Biology Watcher*; Viking: New York; Garnstone: Petworth, UK; for review, see *Nature*, 258, 24; 1975), know how misleading such a first glance would be. In common with another Lewis, Lewis Carroll, he has an extraordinary intellectual exuberance. I have not read any of his papers on pathology (Thomas is a distinguished pathologist) but I guess they are as unlike *The Medusa and the Snail* as Lewis Carroll's *Euclid and his Modern Rivals*, published just 100 years ago, is unlike *The Hunting of the Snark*.

Carroll wrote for children. Thomas writes for grown-ups who still retain a child's capacity for wonder. Apart from his

mastery of prose, which makes me green with envy, he has a rare talent for picking up something familiar and suddenly, with a flash of imagination, giving it a fresh meaning. It's done deftly, like a conjuring trick. It's the technique of a poet. Edith Sitwell used it effectively; she described it once to me as a "leakage of thought" from one compartment of the mind to another. Thomas himself describes it: "finding the marks of remote similarity, points of distant relationship, tiny irregularities that indicate that this one is really the same as that one over there only more important". And in an essay on thinking about thinking he tries to describe the process. The human head, he writes, "is filled alive with molecules of thought called notions. . . flowing at random from place to place, bumping against each other. . . like the paths of Brownian movement". The mind is heated a little, the movement speeds up, there are more encounters, some of the notions dock and lock (notice the imagery of space-travel), aggregates are formed, they act like "purposeful organisms, hunting for new things to fit with. . . turning things over, catching at everything" — and a harmonious idea is generated, with the elegant geometry of a Brandenburg concerto. At that point Thomas' mind takes another leap: why not begin with music "and see what this can tell us about the sensation of thinking".

So far so good: the book is delightful entertainment. Is it more than that? I believe it is. It is a piece of intellectual autobiography. Its theme is the impact of Nature on Lewis Thomas. By what I believe is a valid extrapolation, it speaks for thousands of other less articulate biologists and naturalists; and this is why it is more than entertainment. Thomas visits the Tucson Zoo and watches beavers and otters at play in glass-walled pools. For a few minutes he sheds his professional reductionist shell and becomes, as he puts it, "transfixed. . . there was only one sensation in my head: pure elation mixed with amazement at such perfection". The beavers and otters had done something to

him. "I learned nothing new about them. Only about me, and I suspect also about you, maybe about human beings at large: we are endowed with genes which code out our reaction to beavers and otters, *maybe [my italics] our reaction to each other as well*".

Speculation, bordering on the turbulent territory of sociobiology? Perhaps it is, but there is no dogmatic assertion in Thomas' reflections. He offers you a subjective experience, take it or leave it. I would be surprised if many biologists reject the *credo* which is the main motif in these essays. The *credo* rests on wonder at two principles Thomas finds all around him. One is uniqueness; the other is symbiosis. Here are a few examples of the impact they make on him.

To say that the DNA molecule is the greatest single achievement of Nature is a commonplace opening for an essay. But then Thomas goes on to wonder whether molecular biologists could have achieved this, if they had been flown from another planet to start life off on Earth. Suddenly comes the refreshing insight: "We would have made one fatal mistake: our molecule would have been perfect. Given enough time, we would have figured out how to do this, nucleotides, enzymes, and all, to make flawless, exact, copies, but it would never have occurred to us, thinking as we do, that the thing had to be able to make errors. The capacity to blunder slightly is the real marvel of DNA. Without this special attribute, we would still be anaerobic bacteria and there would be no music. . . it is no accident at all that mutations occur; the molecule of DNA was ordained from the beginning to make small mistakes".

This is the source of the uniqueness of living things, of the idea of selfhood. In the *Testament of Beauty* Robert Bridges came to a similar conclusion along a different path. Thomas takes the scientist's path. He cites the self-labels of beans — the glycoproteins which may negotiate the intimate concordat between bean and nitrogen-fixing bacteria; he cites the capacity of fish and mice to tell each other apart as individuals by a sense of smell; and he concludes that nucleated cells detached from the parent organism seem to be the only living units without a "sense of privacy". It is no wonder he has deep reservations about cloning human beings. Of course, like any other professional biologist, he doesn't think it is likely to happen; but suppose it did: think what this would do to filial affection and paternal care; think of the terrifying prospect of raising from infancy and teaching language and discipline to a creature whose genetic constitution is exactly the same as your own. In any case, as Thomas explains, it couldn't happen because the selfhood of human beings depends not only on their genes but also on their environment, including their personal relations with other human beings, and it would be

impossible to homogenise this environment. And it's as well it couldn't happen, for the only hope for evolution is for the race to have options to be matched against diversity. There's a deep wisdom in the phrase "trial and error"; we don't say (Thomas reminds us) "trial and rightness" or "trial and triumph".

One theme in these essays is to praise uniqueness. The other is to praise symbiosis and cooperation. Uniqueness does not spell solitude. The individuals cannot express their selfhood except in some sort of communication with other individuals. The committee, the quorum, the consortium, the working party: these are not specifically human devices for

overlook another principle governing Nature, namely that decisions, whether consciously made by human beings or unconsciously reached by the mechanism of evolution, are the results of conflicts; and to hold a conflict one has to have an arena, even if it is a committee room.

I have space only to mention a few other flashes of illumination in the book. Thomas knows a lot about linguistics and he points out the difficulties of discussing the meanings of words when the tool for research is words themselves. There is a sort of Heisenberg effect which may distort the argument. Over the applications of science to medicine he is an unashamed optimist. He deplores the American

Sorry, for copyright reasons some images on this page may not be available online

Lewis Thomas

Photo: Helen Marcus

getting things done — they were invented long before by all manner of lowly organisms. Collaboration between organisms of the same kind and symbiosis between organisms of different kinds are so widespread that it leads Thomas to say that "the committee is the basis of terrestrial life". This carries him, at a safe distance from sociobiological analogies, to a discussion of the behaviour of committees of human beings. He has some penetrating things to say about the way we behave on committees. Each member, being unique, "is necessarily an actor, uncontrollably acting out the part of himself, reading the lines that identify him, asserting his identity". This is an obstacle to the efficacy of human committees, not shared by consortia of ants or termites. Each member's function, Thomas says, is to talk, "and while other people were talking the individual member was busy figuring out what he ought to say next in order to shore up his own original position". With more confidence than I myself have, Thomas advocates the Delphi technique invented by the Rand Corporation. His support for it rests on good grounds, namely that the members don't meet; instead they fill out a succession of forms, on which their views are (so it is hoped) modified by the written views of other members of the group. Hence the group members are not in competition to uphold their selfhood; instead they have time to think. Well, perhaps so. But this is surely to

obsession with health: "Get a check-up. Go on a diet. Meditate. Jog". Jogging particularly riles him: "swarms of people, out onto the streets each day in underpants, moving in a stolid sort of rapid trudge, hoping by this to stay alive". Why have people lost confidence in the human body, which has survived plague, starvation, pathogens, and is now better protected from these than ever before in all history? Thomas attributes this obsession in part to the ministrations of an immensely costly health care service.

The book, as I said, is about its author. The scientific content is merely the fuel which ignites his imagination. The personality that emerges is not entirely consistent nor is the argument always entirely logical. Thomas himself will, I think, welcome this comment, for in an essay about schizophrenics he protests that far from being a dreadful thing to have more than one self, it can (if the selves do not crowd into the body at the same time) be a rich experience; and indeed Thomas confesses to being several selves, so he would not wish to be thought to be consistent. And as for logic, Freud had the answer to that one: "Only in logic are contradictions unable to exist; in feelings they quite happily continue alongside one another". □

Lord Ashby is Chancellor of Queen's University, Belfast, and a Fellow of Clare College, Cambridge, UK.

NEW

First Issue JANUARY 1980

COLLOIDS AND SURFACES

Editor-in-Chief:

P. Somasundaran, N.Y.

This new journal is devoted to applications and principles of colloid and interface science. Areas, topics and subjects covered include emulsions, foams, aerosols, detergency and wetting, flocculation and dispersion, rheology, cosmetics, paints, foods, paper and pulp, electrokinetic and electrode phenomena, friction and lubrication, thin films, liquid membranes and bilayers, biomaterials and biocolloids, polymer colloids, pharmaceutical and related health sciences, environmental and aquatic systems, water treatment and dewatering, agricultural and soil science, minerals extraction and metallurgy, precipitation and crystal growth and modification.

Of interest to:

- mineral processors
- petroleum engineers
- soap, cosmetic and textile scientists
- bioengineers
- surface and colloid scientists
- powder technologists
- tribologists

1980: Volume 1 (in 4 issues), \$81.00/Dfl. 166.00 including postage

Write for details or a free sample copy to

Elsevier Scientific Publishing Company, Dept. CLS, P.O. Box 330, 1000 AH Amsterdam, The Netherlands or Elsevier/North Holland Inc., 52 Vanderbilt Avenue, New York, NY 10017, U.S.A. Tel: (212) 867-9040

ELSEVIER

Circle No. 57 on Reader Enquiry Card.

Florey's creative power

E.P. Abraham

Howard Florey: The Making of a Great Scientist. By Gwyn Macfarlane. Pp.396. (Oxford University Press: Oxford and New York, 1979.) £7.95.

THIS book is an authoritative biography of Lord Florey in his early and middle life. It is a tribute to a man who had a central role in the story of penicillin and became one of the great figures in the history of medical science. It is also a product of the persistence of Gwyn Macfarlane, who was told by publishers that an unknown author could not expect to see his biography of a scientist in print unless his subject was already famous in the public mind; and that although Fleming was a household name, Florey was not. Why this was so and how a myth was created are finally discussed in detail. A major theme of the book, however, as its sub-title implies, is the development of Howard Florey as a scientist and the factors that contributed to his success. "To be a great scientist", the author states, "one must (among other things) be a pioneer, a discoverer, a dedicated research worker, and one must be successful"; and he sets out to show how Florey came to fall within this definition.

In his assessment of Florey's character the author, unlike earlier biographers, has quoted from letters that Florey wrote from England and America to Ethel Hayter Reed, a fellow medical student in Adelaide, with whom he thought he had fallen in love. They were referred to later by Ethel as love letters, but *eros* scarcely appears in them although *agape* is sometimes seen. Some of the extracts from this correspondence, between two young people who were fourteen thousand miles apart, seem strangely cautious and business-like. But even those who know the outcome may have a sense of drama and begin to wonder whether marriage will eventually result or not, as problems, difficulties and requirements are laid on the table.

In the event, they married on 19 October 1926 in London a few weeks after Ethel's arrival from Adelaide. The marriage began badly and it was immediately evident that they were unlikely to be perfect partners. She was an attractive woman with intelligence and charm who could write to him on the boat "Do you realise that I shall arrive in England on your birthday: I shall wrap myself up in tissue paper tied with pink ribbon . . . will you accept the present or throw it into the sea?". Yet she was strong willed and difficult to live with and she had

written of marriage as an ordeal. He, like many other young men, had ambition, impatience, idealism and private worries about his capability. They were both unduly concerned by thoughts of a lack of money and, with her, fear of poverty seemed to become almost an obsession. Neither had formed positive views of the nature of their relationship. While he had disclaimed any wish to impede her professional life or press her into domesticity, he had also written: "Married women messing about in labs always appear to be slightly pathological to me".

The marriage was not devoid of affection and there were intervals of contentment which coincided with the birth of two children. But it is clear that he did not find in her the ideal companion of his imagination and that some of her own premarital forebodings became realities. He was exasperated by her increasing deafness; yet other marriages have been happy in the face of greater impediments and the reader is left to wonder whether deeper problems were unresolved.

No general principles to guide the young who aspire to become great scientists are likely to emerge from this topic in the letters, for creative power seems to have been unleashed in some men and stifled in others by emotional frustration. There can be no doubt that Florey's epistolary attachment to Ethel gave him great comfort during his early years in England, when feelings of loneliness sometimes became acute, and that it removed temptation to indulge in diversions which could have interfered with his great enthusiasm for research. But the relevance of his subsequent disappointment to his great achievements is a matter for speculation — a process of which Florey himself was not much enamoured.

The Florey letters, however, also provide a diary of his early years in Oxford, where he obtained a first class in the Honour School of Physiology, and then in Cambridge, America and London. They describe the experiments he had done and intended to do with laboratory animals on the capillaries, the lymphatics, the omentum and mucus secretion. They tell of his emotional response to music and to the architectural achievements of past centuries and give the critical views of a young Australian on the English society of the day. They contain accounts of his meetings with a number of the great or then powerful figures in preclinical medicine, including Charles Sherrington, A.R. Dean, Edward Mellanby and J.B.S. Haldane. And they show that Florey's poor view of the intellectual content of much clinical teaching and of the quality of clinical research had been formed by the time he had qualified in medicine at Adelaide. All this Gwyn Macfarlane brings together in an admirable manner.

It was Sherrington who suggested to Florey that the time had come for an

approach to pathology by a physiologist. Sherrington, Dean and later Mellanby were much impressed by his ability and energy in research and their support helped him to obtain positions at Cambridge and the London Hospital and then Chairs at Sheffield and Oxford. The Professorial appointments were made in the face of powerful opposition, for Florey was not regarded as a pathologist by the morbid anatomists who dominated the profession; Macfarlane tells the well-authenticated story of Mellanby arriving late at a crucial meeting of the electoral board in Oxford to find that it had already been decided to offer the chair to another candidate and of his ability to persuade his colleagues to change their decision. He goes on to describe Florey's frustration during his early years in the Sir William Dunn School of Pathology, his fight for what would now seem to be trivial sums of money for research and his disappointment at finding that the great Nuffield benefaction of 1936 would provide a rich endowment for clinical medicine in Oxford, but do nothing for the pre-clinical departments. But Florey rapidly invigorated what was a nearly moribund Department. He continued his work on mucus secretion and on lymph flow and the function of the lymphatic system. A later outcome of his interest in lymph, when labelling with radioisotopes and other new techniques had become available, was the important discovery by J.L. Gowans of the circulation of the lymphocyte.

Florey's work in these fields, often requiring surgery of great skill and designed to obtain unambiguous answers to straightforward questions, virtually established the subject of experimental pathology in this country. This was one of his great achievements.

The book describes how the research on mucus secretion, which originated from anxiety about his own dyspepsia, led indirectly to penicillin. While still at Cambridge, Florey had become interested in Fleming's lysozyme, probably because the presence of this bacteriolytic enzyme in intestinal mucus raised the question whether lysozyme, or a related antibacterial enzyme, was responsible for the protective action of the mucus. His wish to have lysozyme purified seems to have prompted the thought that experimental pathology would benefit from a collaboration of pathologists with chemists or biochemists. But it was only after he became Professor of Pathology in Oxford that he succeeded in obtaining the funds for a biochemist to work in his Department. It was thus that Ernst Chain, a Jewish refugee from Hitler's Germany who had just finished his PhD at Cambridge and was warmly recommended by Gowland Hopkins, came to the Sir William Dunn School of Pathology in 1935. He worked at first on the mode of action of snake venoms and then, at Florey's suggestion, he turned his attention, with L.A. Epstein, to the mode



Howard Florey

of action of lysozyme.

It has never been possible to write a history of penicillin that would have satisfied all of those who were closely concerned. But in most of its essential features Gwyn Macfarlane's well documented version probably comes as near to the truth as anyone is now likely to get, and it is only his treatment of some of the chemical studies which is open to question. He devotes one chapter to Alexander Fleming and the extraordinary conjunction of chance events (analysed by Ronald Hare in *The Birth of Penicillin*; George Allen and Unwin: London, 1970) that made it possible for him to discover penicillin in 1928. Why Fleming made no attempt to test its ability to cure bacterial infections in mice, as he could have done, is a question to which he never gave a satisfactory answer. There is no evidence for the suggestion of André Maurois, his biographer, that he was actively discouraged by his chief, Almroth Wright. His claim that he lacked chemical help is unconvincing, because he showed little

interest in the work of two young assistants, Ridley and Craddock, who prepared crude extracts of penicillin, and none at all in the later and soon abandoned attempt at isolation by Raistrick, Clutterbuck and Lovell. It seems that the idea of using penicillin as a systemic chemotherapeutic agent simply did not occur to him, nor did it occur to such influential figures as Wright and Topley. But Gwyn Macfarlane rightly says "Fleming should not be criticised for what he did not do" and concludes that his genius for discovery was not accompanied by the sort of character needed to exploit what he found.

Ten years after Fleming's discovery, an investigation of penicillin was begun in the Sir William Dunn School of Pathology, as Chain's work on the substrate of lysozyme led him to make a survey of the older literature on bacteriolytic substances. "Dr Chain and I", wrote Florey, "had many discussions on the possible interest of a systematic and thorough study of the known natural antibacterial substances";

and later he said: "eventually he proposed, and I agreed to go along with it, that we should make a thorough investigation of antibacterial substances. This is why we looked at penicillin". Chain's biochemical interest in penicillin was aroused by its reported instability and Florey was struck by its activity against the staphylococcus, against which the sulphonamides had proved relatively ineffective. However, penicillin was only one of three substances first chosen for study and was at first given no particular prominence. Gwyn Macfarlane leans towards the view that thoughts of "suffering humanity" lay behind the decision to work on penicillin. Florey, however, has stated categorically that this was not the mainspring of the motivation, which was scientific interest, and he did not fail to acknowledge the role of chance: "We happened to hit on an antibiotic which worked in man. We could have worked with hundreds of others and they would have been chemical curiosities".

Florey always maintained that the success of the penicillin project itself, which seemed at the time to be almost miraculous, was due to the combined work of a small group: "I am quite clear that nothing would have gone along except for a group of five or six people". Gwyn Macfarlane gives handsome bouquets to all those concerned in a detailed account of the extraction of penicillin and the dramatic results obtained from well-planned experiments by Florey, first in mice and then in man. But he rightly concludes that it was only Florey's drive and personality that held the group together, and enabled difficulties to be overcome which at first seemed insurmountable in war-time Britain.

Chain made no secret of his view that he had received too little credit and reward for his part in the penicillin story and that the Medical Research Council was guilty of a major error of judgement in not obtaining patent protection for the Oxford work on penicillin. But although it is now widely accepted that a policy which excludes the products of academic medical research from patent cover is a form of idealism that the country cannot afford, this was not so before and during the War. At Florey's suggestion, Chain went to Edward Mellanby, then Secretary of the Medical Research Council. However, Mellanby, who seems to have regarded him as an alien and troublesome personality, was unmoved. The official attitude became the subject of public criticism, but this may have been irrelevant, at least in relation to the achievements in Oxford, because it is by no means certain that a rewarding patent could then have been obtained. Although the results with penicillin were new and far-reaching, penicillin itself was not new and it had not been characterised chemically. The methods used in its production were soon to be superseded by others in America. The most important unpublished step in its

purification (extraction as a salt into water from an organic solvent), which was suggested in Oxford by N.G. Heatley, had already been taken (unknown to him) in 1934 by Lewis Holt, a chemist at St Mary's Hospital whose work was never mentioned by Fleming. Moreover, the penicillin produced later in the United States for clinical use (benzylpenicillin) differed in its side-chain from the penicillin then being studied in Oxford.

The book also contains comments on another aspect of this question. After the clinical trials at Oxford in 1941 Florey decided that American help would be essential for the war-time production of penicillin in quantity. With the agreement of the Medical Research Council and financial support of the Rockefeller Foundation, he and Heatley went to the United States to try to interest the American pharmaceutical industry. Penicillin, then only produced in minute quantities, was far from easy to sell, but Heatley was invited to the Fermentation Division of the Northern Regional Research Laboratory in Peoria to help get a project started. He worked with A.J. Moyer, described in the book as "a fervent anti-British isolationist" with a "positive flair for making moulds do what was wanted". Moyer and Heatley had agreed on a joint publication, but the paper which eventually appeared was in Moyer's name alone. During this time the outlook for penicillin production was revolutionised by the American decision to add corn-steep liquor to the growth medium and to use deep fermentation, and these advances became the subject of American patents. British firms were understandably irked when they discovered that they were required to pay royalties to America to produce a substance that was essentially a British discovery. But equity and patent law may sometimes diverge. At the root of the problem was the fact that the official pre-War world in Britain was entirely unprepared for a situation of the kind that penicillin threw up. And there is, of course, another side to the matter. Without American help it is inconceivable that enough penicillin would have been produced, as it was, to treat all serious battle casualties, British and American, when D-day came in Europe.

The penultimate chapter of the book is headed "Palmarum qui meruit ferat", a phrase used by Almroth Wright in a letter to *The Times* on 31 August 1942 firmly placing a laurel wreath on Fleming's brow. The nature of the publicity that followed can be attributed partly to Florey's refusal to talk to the press, partly to the welcome given to the press by Fleming and others at St Mary's Hospital and partly to the unwillingness or inability of popular writers to acquaint themselves with the facts in the scientific literature. One of these stories, written by a bacteriologist at St Mary's and more ludicrous than others only in the extent of its fabrication, attributed

virtually all that had been done in Oxford to Fleming himself. The source of this myth is uncertain, but Gwyn Macfarlane remarks that behind Fleming were Almroth Wright "intensely ambitious for his department" and Lord Moran, Dean of St Mary's Hospital Medical School "Whose dearest wish was for its honour, glory, and financial security" and suspects that an efficient Public Relations Officer was active somewhere in the organisation. Fleming himself is said to have derived an impish glee from the more bizarre stories as he collected cuttings, a reaction that might have been understandable had he not been gaining worldwide gratitude from their publication.

Florey complained of this situation to Edward Mellanby who replied that it was ephemeral and of little consequence and that "in time even the public will realise that in the development of this story of penicillin, the thing that has mattered most has been the persistent and highly meritorious work of your laboratory". There is now now reason to think that the

publicity has ever affected the judgement of scientific bodies of any consequence, but its effect on the public has been far from ephemeral.

Gwyn Macfarlane finally summarises some of the qualities which combined to make Florey an outstanding figure: his great energy and enthusiasm for research; his skill as an experimenter and commitment to experiments that gave clearcut results; his judgement and sense of direction; and his complete intellectual integrity, never clouded by vanity. His colleagues who came to like and admire him will remember that behind a deep reserve there were kindness and consideration for their welfare. It is to be hoped that this well documented book will make his qualities and great contributions to science and medicine more widely known. □

E.P. Abraham is Professor of Chemical Pathology in the Sir William Dunn School of Pathology at the University of Oxford, UK.

Olduvai record

J. Desmond Clark

Olduvai Gorge: My Search for Early Man. By Mary Leakey. Pp. 181. (Collins: London, 1979.) £6.50.

EAST AFRICA remains unsurpassed in the wealth of discoveries and the understanding these provide about the biological and cultural evolution of our own species. It is no exaggeration to say that the very impressive record of hominid fossils and cultural remains in their palaeo-environmental setting that has come from East Africa and the Horn over the past twenty years, has revolutionised our knowledge of human phylogeny. The hundreds of fossil hominid remains recovered, often remarkably complete and well preserved, and the circumstances of their preservation have made it possible to identify some of the behavioural adaptations that underlie the beginnings of tool-making and the ensuing intellectual development manifest in the increasing complexity of the tool-kits and the economic strategies that gave rise to them.

A very great deal of what is known today results from the lifetime devoted by Louis and Mary Leakey to their search for early man — a search which has completely vindicated Louis' claim, first made when he was an undergraduate at Cambridge in the 1920s, that a wealth of evidence awaited discovery in the deep sedimentary sequences of the Great Rift Valley. It was really the first full season's work in 1935 at the Olduvai Gorge in northern Tanzania, which was also Mary Leakey's

introduction to fieldwork in the African Quaternary, that was the first demonstration of the correctness of Louis' conviction. It was also the first manifestation of his shrewdness — some would say his luck — in having concentrated on the Rift which, as can now be seen, is probably the most significant region in the world for preservation of the Plio-Pleistocene record that spans the emergence and early development of man the tool-maker.

The fossil, geological and cultural evidence is unique, both in its completeness and in the relatively minor disturbance that it has suffered. This has made it possible to reconstruct the changing climatic and ecological conditions under which hominid evolution took place, to find and excavate the activity places of the hominids, and to date all these events. In the 1930s, there was no way of knowing how old the then earliest fossils and stone tools were. At that time Keith's 'guesstimate' of 200,000 to 400,000 years did not seem unreasonable to many and, indeed, most people then thought in terms of half a million or so years for the beginning of the Pleistocene. Now, K/Ar, uranium fission-track dating and the palaeomagnetic reversal chronology show that the earliest stone tools are about 2 million years old; that the earliest, well-known hominid (*Australopithecus afarensis*) is between 3 and 4 million years old; and that even earlier, but fragmentary, remains are present in the East African sedimentary record. From the 1960s onwards, a number of interdisciplinary and international teams have been working in the East African and Ethiopian sections of the Rift and on the adjacent parts of the plateau — for example, at Laetoli, Olduvai, Omo, East Turkana, Hadar, and on the

Ethiopian Plateau. The discoveries and information that this work is producing are of paramount significance and there is every expectation that, as the research continues, an even greater wealth of material, detail and clarification will result.

Dr Mary Leakey's contribution to all this is both very substantial and outstanding in its importance. It was she who pioneered and introduced to Pleistocene prehistory the methods of excavation, recording and recovery that are common practice today. A meticulously careful and observant fieldworker, Mary Leakey found that activity areas were still preserved within the fine-grained sedimentary sequences in the East African Rift where she and Louis worked. She was also the first to demonstrate the existence of these early sites and to apply to them the methods used by archaeologists in the excavation of settlements of much more recent times. By exposing the whole, or large parts of an occupation area to give a complete visual perception of the relationships between all the imperishable residues — artefacts, bone waste, features, hominids, and so on — in their palaeotopographical setting, palaeoanthropologists now have the opportunity of making direct comparisons with the residues resulting from various accumulating and dispersing agencies — geological, chemical, animal or human — and therefore of developing explanatory models for early hominid behaviour.

Since 1959, when she found the first hominid cranium (*Australopithecus boisei*) in Olduvai Gorge, Mary Leakey has worked there almost continuously; and since 1968, she has made her permanent home at the Gorge. The scientific results of her work are recorded in the classic Volume 3 in the Olduvai Gorge Series (*Olduvai Gorge: Excavation in Beds I and II, 1960-1963*; Cambridge University Press, 1971) which is shortly to be followed by a volume on the discoveries in Beds III and IV and the later sediments. Obviously, such works are not the place in which to record some of the more personal events of everyday life at Olduvai — always exciting and packed with activity.

The present book is an attempt to make up for this by telling something of camp life at Olduvai and the way the work there has progressed through her own systematic fieldwork and that of the team of collaborators who have been working with her on the geology, palaeontology and chronology of the Olduvai sedimentary sequence that began two million years ago. For someone wishing for an overall appreciation of the setting in the Serengeti, a record of the main discoveries with something of their significance and an account of some of those involved with the author in the work at Olduvai, the book admittedly fills a need. It is divided into eight chapters, the first seven dealing with the early discovery of the Gorge; camp life; geology, dating and excavation methods;

Sorry, for copyright reasons some images on this page may not be available online

the stratigraphic sequence of sites in their geological setting; the search for the hominids; the nature of the stone artefact assemblages, with a very useful illustrated glossary of terms; the associated animal remains; and the evolutionary changes which the Olduvai record shows that some of these underwent.

The book, however, will not entirely satisfy the reader who looks for a more personal account of the life and work at Olduvai — the problems, stresses, excitements, frustrations and successes of the author's life and search. Her interest in the natural setting, the vegetation and the animals is readily apparent but some readers might, for example, have appreciated a description of the view from

the camp dining room following the remark (page 23) that it is magnificent. Similarly, more might have been made of the opportunity to describe the Masai way of life. The layman would also, no doubt, have found it useful to have had more of the scientific names of the animals, and so on, explained in chapter 7.

On the other hand, the description of the prehistoric living sites and stone tools well conveys the author's particular interest in this part of the work and describes the way in which a living site is laboriously uncovered. Also, some of the excitement and rewards of the work are conveyed by the account of the stone circle which portrays the earliest man-made structure yet known and which was found at the base of the more than 350 foot sedimentary sequence, and also by the description of the more enigmatic 'pits' on a later site. More space might have been given to an account of the butchery sites but prehistorians will find valuable the previously unpublished data on Beds III and IV and the later series of beds.

Regrettably, the hominid footprints found at Laetoli receive hardly more than passing mention and, even though Laetoli is a short way distant to the south of Olduvai, more space might surely have been devoted to this momentous discovery which provides proof of the bipedal nature of Pliocene man.

In the concluding chapter, Dr Leakey discusses the significance of the East African evidence and the great potential that exists there for increasing understanding of the ways of life of the earliest hominids. As she points out, the evidence coming from the African continent is today the most complete for this time period anywhere in the world; this can, in part, be explained by the unique circumstances of preservation and the continuity of research there. The opportunities for fieldwork as well as the circumstances under which fossils were preserved and the possibilities of dating them have not been so good in the Asian tropics. It is, nevertheless, essential to know if an equally long record of hominid evolution also exists there; and it is to be hoped that the field studies now under way will provide at least part of the answer, through the kind of teamwork which has proved so successful at the Olduvai Gorge and which is revealed in this book.

Although the book does not really do justice either to the enthusiasm or the known achievements of its author, it does contain much of interest to all kinds of readers. It remains a record of more than forty years of unparalleled devotion to the search for early man. □

J. Desmond Clark is Professor of Anthropology at the University of California at Berkeley. Professor Clark has known Mary Leakey since 1941, and has worked with her many times since then.

Memories of Sherrington

C.G. Phillips

Sherrington: His Life and Thought. By J. C. Eccles and W. C. Gibson. Pp. 269. (Springer International: Berlin, Heidelberg and New York, 1979.) DM34.

SHERINGTON died in 1952. Within ten years a young collaborator of Ragnar Granit's was confessing that his generation knew nothing about him. Granit's answer was that many of the conceptual foundations of their research were created in Sherrington's mind. His *oeuvre* is remarkable for its sheer coherence. Discoveries and rediscoveries fall into place in an almost continuous narrative, as can be seen in Denny-Brown's *Selected Writings of Sir Charles Sherrington*, now reprinted by Oxford University Press for the Guarantors of the journal *Brain*. These, together with *The Integrative Action of the Nervous System* (1906) and the last chapter of *Reflex Activity of the Spinal Cord* (re-issued recently by Oxford University Press on D.P.C. Lloyd's initiative), are all readily available to anyone who wishes to know and value Sherrington's achievement. He was evidently concerned to leave his scientific testament in good order. Many will wonder at his highly individual literary style, seemingly so contorted in places and contrasting so strongly with the plain English in which he wrote the letters and reminiscences now published in Eccles' and Gibson's book. One has to remember that he was striving to express ideas which were not yet familiar to his readers. R.S. Creed in his memoir explains that Sherrington's first care was to escape ambiguity and to be concise, rather than to be immediately intelligible. The contortions were not casualties of confused thinking, but the result of deliberate rewriting, often delayed by the search for some crucial word. On these foundations neuroscientists are still building, usually as unconsciously as Granit's pupil. Though modest in manner, Sherrington was not quite without vanity: Denny-Brown has told how he "shyly" produced Hamburger's comment (which prefaces *Selected Writings*) that anyone who had witnessed his demonstration of reciprocal inhibition in a monkey at the Fourth International Congress of Physiologists in 1898 "a enrichi sa connaissance pour toujours". But in his preface to the re-issue of the *Integrative Action* (1947: extracts reprinted by Eccles and Gibson) he referred to it as "my rather elderly book". To J.F. Fulton he wrote (when he had just retired, in his late seventies): "Thank you for mentioning again that the old *Integrative Action* still

floats. I know how generously you regard it, and am very grateful. But looked at rigidly I cannot but recognise that it has "had its day". Its best future is for what lives of it to be incorporated — unobtrusively — into what is written with similar scope, now and after, for a time". At about the same period, in his review in *Nature* of Romón y Cajal's autobiography, he quoted the "wistful" passage in which his old friend, whose structural work on the neurone had always complemented his own physiological work, accepted that "the facts associated at first with the name of a particular man end by being anonymous, lost for ever in the ocean of Universal Science. The monograph impregnated with individual human quality becomes incorporated, stripped of sentiments, in the abstract doctrine of the general treatise. To the hot sun of actuality will succeed the cold beams of the history of learning". Sherrington's comment: "We may express this in short by saying that, as Aristotle thought of the soul, a scientific writing has no personal immortality". Yet active scientists do sometimes go to the writings of their forebears for inspiration — a creative act of ancestor-worship.

C.E.R. Sherrington, in his *Memories* now published by Eccles and Gibson, wrote that his father was averse to the idea of any "extensive biography". Sherrington's pupils have respected this wish. In formal memoirs, written at the time of his death, they have recorded the facts of his career and the people who helped and influenced him. Of these memoirs, that by E.G.T. Liddell, in the Royal Society's series, is the acknowledged masterpiece. Liddell's homage took the form of a remarkable book, *Discovery of Reflexes*, in which, with the insights of a neuroscientist as well as those of a scholar who reads seventeenth-century Latin as well as French and German, he painted a splendid landscape of knowledge and ideas about the nervous system at the time when Sherrington began to publish in 1884. This sets in relief the veritably Harveian revolution which Sherrington brought about. Ragnar Granit's *Charles Scott Sherrington: An Appraisal* tells of the modern experimental exploitation of Sherrington's seminal discoveries and concepts: the synapse; central inhibition as an active process; convergence and interaction of excitatory and inhibitory synaptic inputs at the neuronal membrane; receptor organs in muscle and their reflex actions, as proof of their continuing vitality. Eccles and Gibson have also respected Sherrington's wish, though a sentence at the beginning of their Preface (not to mention "the definitive Sherrington biography" proclaimed by the publisher's dust-jacket blurb) might have alarmed him. "More and more, students of history are calling for creative writing on the whole man, particularly when he is a genius. Those interested in the genesis of ideas

want to know the settings for discoveries and the relevant circumstances which ushered in new truths and insights". "Creative writing on the whole man" suggests imaginative reconstruction of feelings and motives and of intimate personal relationships. His visits to Eastbourne left Liddell in no doubt about Sherrington's feelings in his very old age. "Hardly ever, he felt, can a biographer discern and interpret the inner thoughts which have moved the mind of another man years before. The mind made the man, and its achievements alone are worth recording". But Eccles and Gibson's wholly delightful book is not that sort of biography. In the first place, getting on for one-third of the words are those of Sherrington himself, a charming anthology of writings relating largely to life outside the laboratory. In the second, the well-known landmarks of his career are freshly illuminated by quotation from a large collection of letters, which, together with other Sherringtoniana, are housed in Professor Gibson's Department of the History of Science and Medicine in the University of British Columbia. Thirdly, both authors worked in Sherrington's laboratory at Oxford, and now add their personal witness to that of the others who shared in the action during his last years, when, in his seventies, he had steered his reflex experiments away from their significance as items of adaptive behaviour and into the neuronal basis of their physiological production and execution, and had brought them to their zenith of technical refinement and quantitative precision.

The Preface says that the book will concentrate on themes that have been "but lightly touched on" by previous writers. One only of its promises is not performed: one finds nothing about any analysis by Sherrington of the lack of productivity of British medical science at the end of the nineteenth century. For readers whose first love is to do experiments, Eccles' story of his exciting years with Sherrington in the 1920s and 1930s will be the highlight of the book. They were counting the muscle-fibres in the motor units and estimating their average contractile force. (The cautionary tale of the "muscle angle" comes in here). The motor nerves had to be emptied of afferent axons by antecedent dorsal root ganglionectomy. Sherrington was not only skilled in this delicate operation, but was also responsible for the perfectly circular and uncrinkled appearance of the myelinated motor axons in transverse sections; he dehydrated the splinted nerves overnight in his bathroom at home, and spent many happy hours in teasing nerves in order to prove the branching of motor axons. They noted the two peaks in the axon diameter spectrum, but inexplicably, in view of their awareness of the motor innervation of muscle spindles and of Sherrington's discussion of its possible significance in his Linacre Lecture

in 1924, failed to suggest that the smaller-calibre group was fusimotor. Then came the long series of experiments on the interaction of excitatory and inhibitory reflex inputs, testing Sherrington's already-published theories and leading up to their culminating statement in the final chapter of *Reflex Activity of the Spinal Cord*. The atmosphere of the laboratory comes to life as we learn how they recited Keats and Bridges during the routine preparations, how Sherrington spoke of such things as his belief that Verocchio's studio was like a modern research laboratory, and how, on those two strenuous days each week, they missed lunch but went into the town for an enormous afternoon tea before the final recording session.

Eccles' involvement in the mind-brain problem is well known, most recently from his book with K.R. Popper (*The Self and Its Brain*; Springer: Berlin; for review, see *Nature*, 272, 770; 1978), and his Gifford Lectures have also been published by Springer this year as *The Human Mystery*. Sherrington thought deeply about the problem in his last years. In 1922, in his Presidential Address to the British Association (reprinted in an Appendix as *The Times*' report), he spoke in evolutionary terms of the "twilit emergence of mind from non-mind, which is repeated in the individual life-history". His Rede Lecture, *The Brain and its Mechanism* (1933) was "eagerly read" in the laboratory "as giving some glimpse of the philosophical thinking he had been developing unbeknown to us". In his Gifford Lectures, *Man on his Nature*, first published in 1940, and about which, also, he was "secretive" (or dismissive: to Fulton — "I fear they are *not* interesting") he developed these themes in a biological epic of Homeric stature, its whole conception and wealth of illustration the product, as Eccles well says, of one of the most cultivated minds of the modern world. The Lectures were on Natural (as distinct from Revealed) Religion, and the audience, mainly of clergymen, can have received little comfort. Supernatural explanations of biological phenomena — heredity, ontogeny, adaptation for survival — had been replaced by natural explanations or shown to be replaceable in principle. Animate nature is amoral and much of it can only be valued by moral beings as loathsome. Yet, though mindless, its products adapt to pressures which threaten survival in ways which seem purposeful. Then comes the gradual emergence of "recognisable mind", linked with the appearance of bigger and more complex brains, and conferring increasing domination of the environment and of other species. Eventually there appear aesthetic and moral qualities which give hope that altruism will supplant predatory behaviour. "It may likely mean a human future led by women more eminently than by men". Yet neurone and synapse seem everywhere the same; and, in spite of the

essential unity of bodily and mental life, analysis finds *two* modes of activity, mind and energy — irreducibly. Confronted with this twentieth-century epic, different readers will respond differently. Eccles' response, as shown in the passages he has chosen and in his commentaries, follows the lines of his well-known books, but differs for example from Granit's (we may think) equally valid one. One can agree that Sherrington "embraces as equals all the values", but be puzzled by the statement (page 156) that he "even exalts altruism

Sorry, for copyright reasons some images on this page may not be available online

above truth". One hopes that readers will be encouraged to go to the source. Schrödinger wrote: "I cannot convey the grandeur of Sherrington's immortal book by quoting sentences; one has to read it oneself".

Though deadlocked about how mind and energy interact in the brain, and unwilling to propose any hypothesis, Sherrington had written (in the Rede Lecture) "I am not a defeatist, for I would urge active pursuit of the enquiry", though "it seems to me, speaking in all humility, that from time to time the biologist has to make plain how far or near he is from the answer". If "man, the best among us", finds out "how the brain does its thinking", he "will certainly try to improve its ways of doing so . . . We need not be prophets to foresee that then will come the long-told speedy extinction of man. The planet will then be re-liberated, free for the next era of animal domination". Today it seems that the same danger could come from psychotropic substances discovered by chemists, whose control of thought and behaviour might bring extinction before neuroscientists have had time to discover

"how the brain does its thinking".

Professor Gibson's quotations from his collection of letters illuminate the whole range of Sherrington's activities. As a professor, he never had a secretary, but wrote his many letters by hand and kept his files himself, with help from his wife. He could rely on an extraordinary memory. His letter of 1947, describing how his pioneering use of diphtheria antitoxin saved the life of his eight-year-old nephew in 1893 or 1894, is reproduced in facsimile. Although genial he could be firm when necessary — as when the Dean at Liverpool, an anatomist, tried to cut physiology by half and pathology by a third to gain more time for anatomy. He helped many people, notably Harvey Cushing, Wilder Penfield, Hugh Cairns and Howard Florey, in their careers. Private donors gave him money for research. In thanking the British Medical Association for financial support, he drew public attention to the £4,000 per annum which in 1907 was all the Government gave to the Royal Society to support research in all fields in the whole of the British Empire. "The sum is about the same in amount as — sad to say — the average yearly takings of a public-house in a poor quarter of this city". He spent much trouble on public education and in service on committees — writing articles for the *Encyclopaedia Britannica*, six chapters for a manual of school hygiene, reports on health in schools, on the importance of longer hours of sleep in public schools, on tests for sight and colour blindness, and even on the infectivity of oysters. Partly to study industrial fatigue he worked during the long vacation of 1915 (he was 58) in a munitions factory. No-one knew who he was, and the foreman offered to write him a good testimonial. Asked by Alan Gregg of the Rockefeller Foundation about the function of modern Oxford, he replied that it could no longer rely on its centuries-old skills in teaching what is known, but "must learn how to teach the *best attitude* to what is *not yet* known. This also may take centuries to acquire but we cannot escape this new challenge, nor do we want to".

Gibson has a fine chapter on Sherrington the Poet, illustrated by several sonnets and extracts from longer pieces. His work was taken seriously by Hardy, Edmund Gosse and Walter de la Mare. An appendix reprints his undergraduate essay on Longfellow. There is a good deal of correspondence about his lifelong collection of incunabula — another interest about which he was ordinarily extremely reticent. His gifts to the British Museum marked him as its "best benefactor in modern times". Then there is his hilarious account of Christmas at Grindelwald in 1887. And so on. Having read it all you will want to browse frequently. □

C.G. Phillips is Dr Lee's Professor of Anatomy at Oxford and Editor of *Brain*.

Early days of behaviourism

O.L. Zangwill

J.B. Watson: The Founder of Behaviourism. By David Cohen. Pp. 297. (Routledge and Kegan Paul: London and Boston, 1979.) £8.95.

THIS is a biography of Watson; not a study of the origins of behaviourism. Nonetheless, Dr Cohen's well researched and highly readable book tells us a good deal about the early days of behaviourism, a school of psychology which Watson himself once spoke of with evident pride as 'this purely American production'. His account will do much to demolish the still popular myth that behaviourism amounted to little more than the export of conditioned reflexes from Russia to the United States and the substitution of muscle twitches for mind as the subject-matter of psychology. At all events, in so far as conditioned reflexes are concerned, Watson owed distinctly less to Pavlov than to his contemporary and rival, Vladimir Bechterev, whose correspondence with Watson may still be seen at the Bechterev Institute in Leningrad. Moreover, Pavlov himself made no secret of his detestation of behaviourism and ridiculed its pretensions to be a scientific discipline. Pavlov, of course, was a militant physiologist imbued with the materialist philosophy which he had brought from Germany, whereas Watson was a psychologist through and through, concerned only to establish a viable science of human behaviour. It is not surprising that relations between them were cool.

John Broadus Watson was born in 1878 in Greenville, South Carolina. His father was an impecunious farmer and his mother a pillar of the local Baptist community and a Fundamentalist who evidently ruled her family with a rod of iron. Following graduation from Furman University in 1899, Watson proceeded to the University of Chicago, where he came strongly under the influence of James Rowland Angell, a sometime student of William James' who favoured a biological, or as it was then termed 'functionalist', approach to psychology in contrast to the 'structuralist' approach of Wundt, with its emphasis on classification and introspective method, which Titchener and other early experimental psychologists had exported from Germany. Although Watson came later to disown 'functionalism' almost as radically as 'structuralism', he seems to have retained towards Angell himself a deep and abiding respect.

On Angell's advice, Watson began his graduate work in the field of comparative psychology. His PhD thesis, published in 1903 as a monograph under the title of

Animal Intelligence, was largely concerned with the growth of learning capacity in the white rat, with special reference to the medullation of the nervous system. (The neurological aspects of this work owed much to the Chicago neuroanatomist, H.H. Donaldson, who evidently thought highly of Watson and to whose personal generosity he owed its publication.) In this study, it is noteworthy that Watson had no hesitation in using the concepts and nomenclature of introspective psychology, and it belongs much more closely within the 'functionalist' tradition than any of Watson's later publications.

Watson continued with his animal work at Chicago for several years and some of it has proved surprisingly durable. With Harvey Carr, he worked on spatial orientation in the rat, with special reference to kinaesthesia and the sensory control of maze learning. At this time, too, he first made the acquaintance of Karl Lashley, then still a graduate student, and collaborated with him in some early studies of bird behaviour. He also came to know Robert Yerkes, then a young physiologist at Yale, who became a firm colleague and friend. From Dr Cohen's account, it might be surmised that, had Watson remained in Chicago, it is by no means impossible that the scandal which was later to drive him out of academic life would have been averted.

In 1908, Watson became a full Professor of Psychology at Johns Hopkins University, and it was at Baltimore that behaviourism was born. No doubt the sympathetic biological climate of this University, and more especially its Medical School, contributed to this happy event, but by far the most important determinant was the advent of Lashley as a PhD student in zoology and psychology in 1911. Although Watson's background in animal psychology and, above all, his total disillusionment with the current schools of experimental psychology, no doubt touched off the behaviourist revolution, without Lashley it seems unlikely that behaviourism would have evolved as a credible competitor or achieved a measure

of real scientific distinction. It was these two men working in close association who virtually created the behaviourist movement.

What, then, was the behaviourist position? This Dr Cohen outlines in two substantial chapters, adequate though philosophically less sophisticated than the account given by Dr B.D. Mackenzie in his recent book on *Behaviourism and the Limits of Scientific Method* (Routledge and Kegan Paul: London, 1977). It may be briefly summarised as follows. First, Watson had already proclaimed that psychology is (or should be) 'a purely experimental branch of natural science whose theoretical goal is the prediction and control of human behaviour'. There seems little doubt that Lashley was fully in accord with this view. Secondly, both men insisted that introspection, for so long viewed as indispensable to the analysis of mind, has no place in behaviourist psychology; nor is the value of its data dependent 'on the readiness with which they lend themselves to interpretation in terms of consciousness'. Lashley later devoted two important papers to justifying this contention. Thirdly, behaviourism was in keeping with traditional Darwinism in so far as it recognised no sharp distinction between the behaviour of animals and that of man. At the same time, it must be borne in mind that, despite the preoccupation with animal behaviour which seemed almost to obsess the behaviourists, it was the understanding of human behaviour which Watson came increasingly to regard as the primary objective of psychological science.

In his seven years at Johns Hopkins, Watson was somewhat less active in personal research but successful in building up a Department of high standing in its field. He was particularly interested in developing detailed observational study of the development of behaviour in young children, particularly their emotional reactions, in connection with which he drew inspiration not only from Pavlov but, more surprisingly, from Freud, whose observations on infantile sexuality par-



Watson at Johns Hopkins, testing an infant's reflexes



Photos: Johns Hopkins University Archives

ticularly impressed him. Much of this work was carried out by his graduate students, one of whom was Rosalie Rayner, later his second wife, and some of their work was reported in *Psychology from the Standpoint of a Behaviourist* (1919), by far Watson's best book. It is odd that an important paper on conditioned emotional reactions in children, written in collaboration with Rayner, is not cited in Watson's bibliography as given in the present book.

In 1920, Watson featured in a divorce case which brought him considerable notoriety and entailed his enforced resignation from his Professorship. The whole sorry story and its attendant circumstances are fully described by Dr Cohen and it is of some interest to note that E.B. Titchener, a conservative Englishman who for many years represented the Wundtian tradition in America and who had no use whatsoever for behaviourism, was one of the very few professional colleagues who stood by Watson after his fall from grace. In spite of Titchener's support, however, Watson was never again offered a University post and resigned himself to a career in advertising, in which, however, he seems to have been strikingly successful. He also wrote a number of popular articles concerned with child upbringing and education, some of which won the approval of Bertrand Russell, who had himself experienced academic rejection at first hand and was no stranger to the devastating smugness of many American academic institutions some fifty years ago.

The only serious scientific work which continued to engage Watson after his resignation from Johns Hopkins was his observational work on young children. Although much of this was undertaken by a devoted co-worker, Mary Cover Jones, the ideas were undoubtedly Watson's and the work resulted in several interesting, if desultory, publications. Today, this work is of interest largely as the forerunner of what has come to be known as behaviour therapy, which has become a major industry in clinical psychology. Watson, however, did no more than adumbrate the theory and methods of behaviour therapy; its systematic development is the work of others more recent.

Had Watson remained active in psychology, one may hazard the guess that behaviourism would have run a very different, and perhaps more fertile, course. In particular, the obsession with learning theory which infected American psychology in the 1940s and 1950s, and in attenuated form is still with us today, might have proved altogether less dispiriting. On the other hand, the neurological element in Watson's thinking, later developed with such distinction by Karl Lashley, might well have taken earlier and firmer root in American psychology. The advent of behaviour therapy, too, might well have taken place sooner, and been less

disfigured by empty 'scientism' and doctrinaire rejection of Freud and all his works. Finally, a tradition of research on human development might have grown up in America well before Piaget became the monolithic institution that he is today. As a "purely American production", Watson's behaviourism had a genuine feel for biology and a healthy freshness and enter-

prise in tackling the problems of experiment in the sphere of mind. Like many other American products, unfortunately, Watsonian behaviourism failed to survive the Depression. □

O.L. Zangwill is Professor of Experimental Psychology in the University of Cambridge, UK.

Skinnerian behaviour

Stuart Sutherland

The Shaping of a Behaviorist. By B. F. Skinner. Pp. 373. (Alfred A. Knopf; New York, 1979.) \$12.95.

To the general public B. F. Skinner is perhaps the best known experimental psychologist. He has attained fame by repeatedly asseverating the principle that all behaviour is governed by reinforcement, and by his sinister but well intentioned suggestion that we should engineer everyone's environment from birth to produce desirable behaviour. The second volume of his autobiography, *The Shaping of a Behaviorist*, describes his life between the ages of 26, when he entered graduate school at Harvard, and 45, when he became a Harvard professor. The title is misleading: the book in fact fails to reveal the schedule of reinforcement that deflected the young Skinner from his interest in English literature and turned him into a Behaviourist so extreme that he denied the existence of mental events. Unfortunately he abides by his own precepts, and gives no hint either of his own feelings and emotions or of those which actuated the numerous colleagues, acquaintances and girl friends who appear in these pages. In consequence, the book resembles a set of scientific protocols in which events are meticulously recorded but all speculation about cause and effect is avoided.

Skinner's professional success is in part due to his capacity for disciplining himself and for making the utmost use of his talents. He seems rarely to have had an idea that did not eventually appear in print: his book on verbal behaviour was planned ten years before it was written. His substitute for prayer was to write stern notes to himself: when he was thirty he prepared a document entitled "Plan of the Campaign for the Years 30-60" which ends with the frank acknowledgement "Plan for the Years 60-(?). These are beyond my present control". To explain how such elaborate exercises in planned self-control are learned would be a nice challenge to his own theory.

The period of his life described was by

no means an easy one. It is true that he gained a prestigious Junior Fellowship at Harvard, but finding academic positions in the Depression was difficult and he was forced to exile himself to the University of Minnesota and subsequently to Indiana before returning triumphantly as a full professor to Harvard in 1948. During the War he attempted to train pigeons to guide a missile on to its target, but the idea was never taken up by the military authorities. He brought his second daughter up in a specially designed crib, but his attempts to market the "Heir Conditioner" were unsuccessful. Moreover, much of his early work on animal learning met with little acclaim and was overshadowed by the grandiose theorising of Hull and Tolman.

From an early age Skinner set himself against theorising: he was interested only in finding some behaviour that would vary in a quantitative way with changes in the controlling factors. For him the discovery of such a lawful relationship was enough, and he showed little concern over the novelty or importance of his findings: indeed in the absence of a theory, there can be no criteria for what is an important finding.

Nor did Skinner open up any

Sorry, for copyright reasons some images on this page may not be available online

fundamentally new areas of investigation, with the exception of the effects of different schedules of reinforcement: even this work led less to the discovery of new principles than to the elaboration of his basic postulate of reinforcement. If a rat is not rewarded for pressing a bar until one minute has elapsed since the last reward, it learns to press infrequently for a time after reward is delivered and more frequently towards the end of the one minute interval. Skinner explained this result by pointing out that only bar presses made after one minute has elapsed will be reinforced, and hence the animal will come to give more responses after that interval and fewer immediately after reward; the nature of the timing processes that underlie such behaviour was of no interest to him.

Within the limits that Skinner imposed on his own thinking, he often displayed considerable ingenuity. He was amongst the first to distinguish clearly between the classically conditioned Pavlovian reflex and 'operant' responses in which reward is made contingent on the occurrence of the response. He also showed great skill in the design of apparatus for the automatic recording of behaviour, though at the expense of restricting the behaviour recorded. He does not make it altogether clear whether the famous Skinner box was an attempt to make the recording of behaviour more objective or whether it was a device to enable him to carry out more experiments with less effort.

It is interesting to speculate how Skinner's impoverished view of the task of psychology came to attract so wide a following. His insistence on quantitative results may have appealed to those who wanted psychology to attain the respectability of a science; his doctrine of the malleability of man fitted the prevailing ethos of self-improvement in America; his insistence that what was inside the organism was the 'province of physiology, whereas psychology should concentrate on the whole organism gave psychology status as an independent discipline; and his concentration on the role of reinforcement to the exclusion of all other problems obviated the difficulty of thinking about such complicated questions as how the organism stores or retrieves information.

Psychology is now a very different subject and the study of mental processes is once more fashionable. The next volume of Professor Skinner's autobiography will doubtless record how his fame amongst the general populace spread at the time his influence on the academic community was waning. One can only hope that he will relax his professional austerity sufficiently to tell us not only what happened but how he felt about it. □

Stuart Sutherland is Professor of Experimental Psychology at the University of Sussex, Brighton, UK.

The Cardinal Sin

Ann M. Clarke

A. D. B. Clarke

Cyril Burt: Psychologist. By L. S. Hearnshaw. Pp. 370. (Hodder and Stoughton: London; Cornell University Press: Ithaca, New York, 1979.) £8.95.

THIS is a book about an eminent psychologist who committed the scientist's cardinal sin, deception and fraud, during a long productive life which brought him nearly all possible distinctions except Fellowship of the Royal Society.

He is to be condemned not for the views he espoused, many of which we share albeit in a less extreme form, but for his irregular conduct over many years. On the penultimate page of Sir Cyril Burt's biography the author writes:

"It would be totally unfair for a final judgement on Burt to focus on his deceptions to the exclusion of all his positive achievements. He was not, perhaps, either by training or temperament a scientist. He was too impatient to reach, and too confident of having reached, firm conclusions which became for him very early in his career, articles of almost religious faith to be defended at all costs. Yet he brought to psychology many conspicuous gifts..."

Be that as it may, his major claim to fame certainly outside his profession, was his work on the heritability of intelligence, and in this connection many distinguished scientists on both sides of the Atlantic accepted his findings on the assumption that the data as reported were sound.

This beautifully written and well researched book records the life and works of an often charming, sometimes generous and kind, always erudite yet unscrupulous man who deserves a high place in science's rogues' gallery. In 1905, while reading classics at Oxford, he recorded in his diary "My purpose in life concerns primarily myself. It is to produce one perfect being for the universe", and went on to list the necessary virtues. Regrettably he failed to follow his own precepts. Shortly after graduation he was appointed assistant to Charles Sherrington at Liverpool. He remained there five years, commencing his research career and gathering his first data to prove that what he called "general cognitive ability" was innate. As Professor Hearnshaw notes:

"Inadequate reporting and incautious conclusions mark this first incursion of Burt into the genetic field. We have here right at the beginning of his career, the seeds of later troubles."

In 1912, with a reputation already firmly established and on the recommendation of Spearman and Sherrington, Burt was appointed psychologist to the London County Council on a half-time basis. Spearman

had written:

"I can add that he is considered by most experts to be the most brilliant and promising of the younger generation of psychologists in the British Isles..."

Burt seems to have worked indefatigably to collect data on abilities and attainments of London school children and on the development of mental and scholastic tests for their assessment.

Appointed in 1922 to a half-time post in the National Institute of Industrial Psychology to organise its vocational department, Burt remained there for two years and among other things taught some of his colleagues to 'estimate' the IQs of adults without actually testing them! In 1924 he was elected to a part-time Professorship of Educational Psychology in the then London Day Training College, later to become the Institute of Education.

In 1931, aged 48, Burt succeeded Charles Spearman in the Chair of Psychology at University College, London. During the next thirty years, factor analysis became his major interest. He began to make claims to priority as first user of this method, but these were at once retracted when Spearman challenged him. With the latter's death in 1945, however, Burt began to rewrite the history of these statistical techniques, dethroning Spearman as their originator. In a number of publications, especially from 1947 onwards, he began "to make claims about his own early work which were demonstrably contrary to the truth" (page 173). Far from having followed Spearman's lead, he now alleged that he had pursued a different route, and that he was in disagreement with Spearman from the start, a view belied by extant correspondence between them. Later "the claims got more and more extravagant". As Hearnshaw notes, there is a pathology here, of which we could ourselves offer further examples.

Burt retired from his Chair at University College in 1950, after unsuccessfully trying to influence the appointment of his successor. His subsequent attempts at interfering with the running of the Department ultimately led to his exclusion from the College on the decision of the Provost who had earlier warned the new incumbent against allowing Burt any access. The twenty-one years of retirement witnessed a surge of publications on a major theme, the importance of genetic factors in human ability and the unimportance of environment. His most influential papers were all published in journals with which he had a close personal connection. As founder and editor of *The British Journal of Statistical Psychology* from 1947 to 1963 and later as assistant editor, he used it as a frequent outlet. His gross abuse of editorial powers was to some extent known at the time, at least to people like

ourselves around London. Apart from publishing 63 articles under his own name, he frequently altered authors' texts without permission, often misrepresenting their intention and adding favourable references to his own work. In addition "Of the more than forty 'persons' who contributed reviews, notes and letters... well over half are unidentifiable, and judging from the style and content were pseudonyms for Burt" (page 245).

Burt could also be kind and generous, as he usually was to us; Hearnshaw records many tributes from former colleagues and students. He could equally be autocratic and vicious towards, for example, a close colleague to whom he wrote a barrage of memoranda and letters pouring scorn on his research. All this to someone to whom staff and students were deeply attached, and upon whose devoted labours the functioning of the Department largely depended (page 143).

With his undoubtedly brilliant mind and wide educational and clinical experience, Burt became from the 1920s and onwards much in demand for evidence and advice on a variety of practical problems. Hearnshaw suggests that he influenced the developing pattern of English education, as well as contributing to policy in such fields as mental deficiency, delinquency and War Office selection procedures.

So far as any scientific theory is concerned it matters little whether Burt's claim to possess a vast store of data on the intellectual status of relatives was true; their poor quality and many anomalies in reporting were outlined in three independent publications in 1974. However, when in 1976 Dr Gillie of *The Sunday Times*, with our support, charged Burt with fraud there were strong protests. Such charges, particularly in connection with his sample of monozygotic twins reared apart (unique both in size and in extent of environmental differences, mainly reported in the 1950s and 60s) could, however, be made with impunity once Dr Gillie's fairly extensive enquiries had established that Burt's alleged collaborators, Margaret Howard and J. Conway, existed in no relevant records, nor were they known to colleagues at University College nor to his secretary/housekeeper. Space precludes a detailed account of Hearnshaw's later careful researches in connection with the charges; in his endeavour to be both brief and balanced, he has omitted many of Burt's conflicting stories to interested scholars during the last few years of his life, confining himself to a small but adequate sample.

Hearnshaw presents overwhelming evidence

"that neither Burt nor any of his alleged assistants carried out any field work after 1955, and it is probable that all his data, such as it was, had been collected prior to his retirement in 1950, most of it, indeed, prior to the Second World War. Burt certainly

added no data himself after leaving University College, and there is no evidence of any contact or communication with any assistants" (page 239).

Moreover, he did not have, as he frequently alleged, material stored there.

The biographer acknowledges the possibility that the data simply did not exist, but writes:

"Assuming that the data were collected in the first instance, and there seems reasonable grounds for thinking that at least some was, what happened to it? The answer almost certainly, is that the bulk of it was destroyed during the war."



The evidence in support of this conclusion is less than convincing, and includes a letter from Burt to University College written from Aberystwyth in February 1941, requesting permission to store

"files of case-histories of defective, neurotic and delinquent children, rather large collections of children's drawings, compositions etc. systematically gathered while I still had access to London schools..." (page 248).

There is no mention of twin data nor any other material relating to intelligence test results for relatives. Whatever the truth of the matter, one thing is certain: as we pointed out over two years ago, the unknown Miss Conway did not double the size of the separated monozygotic twin sample, between 1955 and 1958, as 'she' and Burt claimed, nor were any further cases examined thereafter. Furthermore, it seems safe to assume that whatever data Burt may once have collected on various kinship correlations these, as M. McAskie (Hull) and more recently D. Dorfman (Iowa) have contended, were not available to him at the time of writing his seminal papers.

It is also clearly established that information on declining educational

standards said to have been compiled by another unknown lady, Miss M. G. O'Connor, which included surveys carried out in 1955 and 1965 (discussed in the 1969 *Black Paper* and in the *Irish Journal of Education*) "were at least in part fabricated" (page 259).

Hearnshaw takes issue with those who like ourselves would dismiss Burt altogether on this evidence, pointing to the esteem with which he was held almost universally in the early stages of his career, and by many up to the time of his death. Among these were two of our former teachers, who we believe would never have expressed their approval had they known what is revealed in this book. The author alludes to Burt's use of short cuts, yet maintains that his contribution to applied psychology was important and must be taken into account in the final evaluation. We have reservations about this conclusion. For example, we have a little known report, published in 1924, in which he states that by means chiefly of psychological and educational tests, he had made an intensive study of backward children. "During the four weeks covered by my visit to Birmingham I personally tested 562 children. This was at an average rate of rather over ten minutes to every child". The psychological examination which he personally undertook used "chiefly the Binet-Simon tests of intelligence revised for English children". From our own extensive experience of testing such children we find this a disturbing example of taking short cuts, particularly as Burt was subsequently regarded as an authority on *The Subnormal Mind*. Later advances in this applied field in fact owed virtually nothing to him.

We cannot recommend too strongly this scholarly yet easily read biography. For this reason we refrain from comment on the well researched and fascinating suggestions concerning Burt's pathological personality and why he behaved as he did. This must have been a difficult book to write, partly because Burt was in Professor Cohen's words "a polymath of Renaissance dimensions"; partly because it was originally commissioned by Burt's sister who, after the public charges made against her brother, remained "convinced of Cyril's integrity"; and partly because of the heavy responsibility for sifting the evidence and arriving at an acceptable account of the life and works of an eminent psychologist who inspired devotion in some and distrust in others.

Two disturbing questions remain. First, why were Burt's deceptions unrecognised for so long? Second, is this case unique in our time? □

Ann M. Clarke is Reader in Educational Psychology in the Department of Educational Studies, and A. D. B. Clarke is Professor of Psychology at the University of Hull, UK.

Organic Stereochemistry

Henri Kagan

In this concise treatment of organic stereochemistry, the author makes few assumptions about the student's previous knowledge, but eventually reaches a level of understanding suitable for most graduate students.

Stereochemistry constitutes an area of chemistry which, if not a distinct science, is an area which can be conveniently treated as a unit. The subject developed within the discipline of organic chemistry and is permeated by the ideas of organic chemistry. However, with the development of effective methods of studying chemical compounds in the solid state, inorganic chemistry has acquired a distinct and comparably large stereochemistry of its own which is better treated separately. Hence it has been necessary to give this text the title 'organic' stereochemistry.

Paper £4.95

Electronic Logic Circuits

J. R. Gibson

The growing use of electronic logic circuits is leading to the introduction of courses at an early stage of degrees in electrical engineering. This text places its emphasis on applications of logic circuits and on design techniques which lead to reliable circuits. This treatment will also be useful to qualified engineers who have not specialised in the subject but who occasionally wish to incorporate simple logic circuits into a system.

Paper £3.95

Elementary General Relativity

C. Clarke

General relativity is becoming popular both in undergraduate mathematics courses and as a subject for research. Although there are many texts concerned with the less advanced concepts of special relativity, this is the first dedicated to providing a suitable background in general relativity for students and researchers.

Paper £5.95

Publication December



Edward Arnold

41 Bedford Square,
London WC1B 3DQ.

Phenomenon of human culture

Edmund Leach

Cultural Materialism: The Struggle for a Science of Culture. By Marvin Harris. Pp.381. (Random House: New York, 1979.) \$15.

THIS is the sixth substantial book that Harris has published since the beginning of 1964. It would be unfair to say that to have read one is to have read them all but certainly there is a great deal of repetition. In the present case the author himself points out (page 77, footnote) that chapter 4, "The Scope of Cultural Materialist Theories", is a partial synopsis of his textbook *Culture, People, Nature: An Introduction to General Anthropology* (1971). Other familiar arguments derive from *The Rise of Anthropological Theory* (1968), *Cows, Pigs, Wars and Witches: The Riddles of Culture* (1974) and *Cannibals and Kings: The Origins of Culture* (1977), but have also appeared in various shorter productions. Second and third time round Harris has not modified any of his positions in response to the chorus of criticism from professional colleagues. Instead he stridently proclaims that he has been misrepresented and then counter-attacks in like measure.

The book is in two parts. Part 1, "Cultural Materialism as a Research Strategy", summarises Harris' position and only just falls short of claiming that Harris himself will prove to be as significant for the history of anthropology as Darwin has been for the history of zoology. Part II, "The Alternatives", contains chapters labelled "Sociobiology and Biological Reductionism", "Dialectical Materialism", "Structuralism", "Structural Marxism", "Psychological and Cognitive Idealism", "Eclecticism", and "Obscurantism". Collectively these "isms" are all embracing and there are few contemporary anglophone or francophone social or cultural anthropologists of any reputation, either distinguished or undistinguished, who do not get an adverse mention somewhere. Indeed, Harris manages to convey the impression that all current forms of anthropological theorising other than his own are completely worthless. For anyone who already knows the facts of the matter most of this shadow-boxing is extremely boring but Marshall Sahlins, whose long review of *Cannibals and Kings* in the *New York Review of Books* provokes repeated anathemas, must be quite delighted to have

got such a rise out of his victim.

It is useless for a reviewer to comment in any detail upon these exercises in academic abuse. Harris conducts a one-sided shouting match against named but inaudible opponents, but if one takes the trouble to discover what these opponents actually said it nearly always turns out either that the other side has much the stronger case or else that Harris' sarcasm completely misses the point. No doubt there are many of Harris' undergraduate readers who will only be too delighted to learn from a senior Professor that they need not bother to try to understand the mathematical, transformational intricacies of Lévi-Straussian structuralism because it is all a lot of nonsense anyway; but, to the initiated, all that Harris manages to demonstrate in this particular chapter is that he himself has completely misunderstood Lévi-Strauss.

The attack on the structural marxists has a more personal twist. In the first place Harris wants to persuade his readers that Cultural Materialism is a sort of improved Marxism with the Hegelian dialectic left out! But besides that, in attacking the 'idealism' of the structural marxists, he is also trying to get his own back on former colleague and pupil Marshall Sahlins and Jonathan Friedman, both of whom have treated Harris' earlier publications with mocking disrespect. But here again most readers are likely to feel that Harris gets much the worst of the argument. And so it goes on. No doubt some of the targets for Harris' boomerangs deserve to be hit, but his scorn is so indiscriminate that the only impression that survives is astonishment at Harris' personal vanity and lack of scholarly judgement.

So what is at issue? In part it is a very old argument indeed. Harris' favourite jargon which opposes 'emic' and 'etic' approaches to culture is only a rehash of the mediaeval disputations over the existence or non-existence of universals which divided the realists from the nominalists. Here Harris' support for an 'etic' position entails a realist universalist doctrine, which is curious in view of his otherwise passionate antipathy to the metaphysics of idealism in all its forms. In other respects Harris' creed is the unsophisticated materialism of the mid-nineteenth century, the standard definition of which is "the view that all facts (including facts about men's minds and wills and the course of human history) are causally dependent upon physical processes, or even reducible to them". Harris is obsessed with the idea that the anthropologist's essential task is to elucidate the causes which have produced the phenomena of human culture as they can now be observed and as they have occurred in history. He believes further that these causal sequences have been simple rather than complex and that the underlying causal principles can be discovered by *a priori* reasoning concerning energy inputs

and outputs without any reference to the fine details of historical or archaeological evidence. In Harris' view virtually all the diverse peculiarities of human culture can be "explained" by taking close note of such "empirical" factors as ecology, protein resources, and population density; but, above all, a universally valid economic law of nature will ensure that historical development will proceed in such a way that, in the long run, a minimax principle will govern the balance of cultural costs against cultural benefits. Harris seems to regard this principle as a sort of anthropologist's equivalent to the second law of thermodynamics; but, as Sahlins has pointed out, it is simply a value judgement among other value judgements and closely akin to the profit motive which so many of Harris' neighbours on Manhattan Island also consider to be a law of nature. Just how far Darwin was right in this regard on the issue of biological evolution is still an open question, but Harris' support of Adam Smith's earlier contention that, in free-for-all economic competition, efficiency will always win out against both politics and morality is mere mysticism.

Harris' professional colleagues disagree with him on a great variety of issues. I can mention only a few. Most of us would hold that in the absence of detailed historical records it is just as difficult to reconstruct the past as to predict the future, so that anthropologists will be well advised to devote their energies elsewhere. Harris' exercises in conjectural history are no doubt very satisfactory for that wide class of general reader whose members want to believe that everything is very orderly and simple and that everything that has ever happened in history is quite easily understood if only we apply the most simplistic principles of common sense; but it does not seem likely that there can be many members of the scholarly professions who would take that line.

Another major objection that has been raised against Harris' work is his irresponsible misuse of the limited historical evidence at his disposal. Any ordinary non-anthropological reader of Harris' books must get the impression that it is an unambiguous, fully established, historical fact that at the time of the Spanish conquest of Mexico the ordinary diet of ordinary Aztecs was desperately deficient in animal protein. Harris in fact claims that it is this dietetic deficiency which provides a "scientific" explanation for the uniquely elaborated institution of cannibalistic human sacrifice among the Aztec. But in fact there is no clear evidence that human sacrifice and cannibalism were closely associated among the Aztec or that the Aztec were ordinarily any more deficient in animal protein than most human populations at most periods of human history.

Complaints of this sort can be raised against almost the whole of Part I of Harris' book. He exhibits *Cultural*

Materialism as a crudely simplified theory of law-bound social evolution which most professional anthropologists are likely to find even less convincing than that offered by Morgan in *Ancient Society* (1878). The theory is not derived from any ethnographic evidence; ethnography is only brought in as illustration, but often in such a slap-dash way as to be totally misleading. For example, around page 104, Harris is discussing his theory of the origin of the state, which is heavily dependent upon the theory put forward by Wittfogel in 1957 concerning the significance of large scale irrigation works for the formation of centralised forms of administration. "It seems likely", writes Harris, "that there was a causal relationship between the size and importance of irrigation systems and the degree of centralisation of political power". He then illustrates this thesis by the examples which Wittfogel himself used: Nile Valley, Yellow River, and so on. But how likely is likely? How large is large? Harris never tells his readers that the earliest large scale irrigation system so far identified by the archaeologists is in Highland New Guinea, a discovery which runs entirely counter to the whole of Harris' *a priori* argument!

Nor is it only on technical issues of anthropology and archaeology that Harris seems at times to be almost wilfully careless. Harris would like his readers to believe that he is well grounded in the philosophy of science. At pages 13-14 we are given a one paragraph summary of logical positivism which is described simply as "a movement which arose in Vienna" (no names; no dates). Two pages later we are told that the verification principle of the logical positivists has been "severely attacked in recent years" under the influence of "the English philosopher Karl Popper". Needless to say *Logik der Forschung* (1935) is cited only in the English edition of 1959. For a scholar who makes such a fuss about the importance of origins and causal sequences this is surely a very astonishing way of presenting the complicated history of the Vienna Circle of which Popper himself was, almost from the start, a very influential, though peripheral, member.

This book will not add to Harris' professional reputation but, regrettably, the cheap sarcasm which Harris directs against the serious arguments of his colleagues often makes a good read. Consequently it may well reinforce the illusion created by Harris' other books that social/cultural anthropology is not a serious academic pursuit at all and that explanation in these fields exists only at the level of Kipling's *Just So Stories*. Some anthropological writing is like that, but not all. □

Sir Edmund Leach is Professor Emeritus of Social Anthropology in the University of Cambridge, UK.

For publication in December:

Fundamentals of Mycology

Second edition

J. H. Burnett

A revised and updated edition of an established textbook which was the first to depart from the traditional taxonomic treatment of the fungi and deal with the general features of the group as a whole.

Reviews of the first edition:

'This scholarly book is almost breathtakingly comprehensive . . . Such is its vision and scope that few mycologists will fail to profit from reading it, whatever their special areas of interest.' — *Transactions of the British Mycological Society*.

'A remarkable synthesis of ideas and data in what is now a vast subject area . . . the book presents a clear coherent picture of our current state of knowledge.' — *Journal of Biological Education*.

'A unique and masterly book that everyone who wants to know about or work with fungi should possess.' — *The New Phytologist*.

Paper £16

Social Behaviour in Primates

Neil Chalmers

Contemporary Biology Series

This area of study has expanded rapidly in recent years and Dr Chalmers provides a conceptual framework within which he organises the available facts. He discusses three different aspects of primate behaviour, namely infant development, sexual behaviour and dominance, and concludes by examining critically adaptive explanations of primate social behaviour and comparisons of human and non-human primates.

Paper £6.50

Field and Laboratory Exercises in Ecology

S. D. Wrattan and G. L. A. Fry

This book represents the first practical integration of quantitative exercises in plant and animal ecology. Fifty-six exercises, grouped in pairs of complementary field and laboratory experiments and arranged round five major ecological themes, are worked through in full detail and a further 150 variations, some suitable for long term projects, are offered.

Paper £7.50



Edward Arnold

41 Bedford Square,
London WC1B 3DQ

Gaia and creative evolution

René Dubos

Gaia: A New Look at Life on Earth. By J.E. Lovelock. (Oxford University Press: Oxford and New York, 1979.) £4.95.

I HAVE always disliked the expression "Spaceship Earth" to designate our planet and I believe that it has led to faulty thinking about environmental problems. The word spaceship calls to mind a mechanical structure carrying a limited supply of fuel for a defined trip and with no possibility of significant change in design. The Earth, in contrast, has many attributes of a living evolving organism. It constantly converts solar energy into innumerable organic products and increases in biological complexity as it travels through space. I was therefore much interested when Jim Lovelock suggested in *New Scientist* in 1975 that the surface of the Earth behaves as a highly integrated organism capable of controlling its own composition and its environment. He used the name of the Greek Earth goddess Gaia to symbolise this complex biological behaviour of the Earth. Lovelock has now developed the Gaia hypothesis in a book that I have read with immense pleasure. I shall first briefly summarise its factual contents, then formulate a few questions in the hope that they will lead to a further development of the hypothesis.

It is not the first time that the Earth has been regarded as a living organism. In a book entitled *The Land Problem*, Otis T. Mason, one of the early American environmentalists, wrote in 1892, "Whatever our theory of its origin, the earth may be discussed as a living, thinking being . . .". The Gaia hypothesis is more concrete and can best be formulated in Lovelock's own words: "The physical and chemical condition of the surface of the Earth, of the atmosphere and of the oceans has been and is actively made fit and comfortable by the presence of life itself. This is in contrast to the conventional wisdom which held that life adapted to the planetary conditions as it and they evolved their separate ways."

The Gaia concept has its origin in the fact that the chemical composition of our atmosphere is profoundly different from what it would be if it were determined only by lifeless physicochemical forces. In an Earth without life, purely physicochemical phenomena would produce for example an atmosphere containing approximately 98% carbon dioxide with very little if any nitrogen, whereas the corresponding figures for our atmosphere are

approximately 0.03%, 79% and 21%. Lovelock presents numerous other examples of such profound departures from chemical equilibrium and postulates the existence of a global force which is able to bring about and keep fairly constant a highly improbable distribution of molecules. He believes that this hypothetical global force consists of the countless forms of life which create and maintain states of disequilibrium through cybernetic systems. Some of these are described in the book. As I do not have the competence to evaluate the validity of Lovelock's physicochemical arguments, I shall restate the problems he discusses in biological terms with which I am more familiar.

The fitness of an organism to its environment is, of course, an essential condition of its biological success and even survival. All living things seem to be endowed with a multiplicity of mechanisms that enable them to achieve fitness by undergoing adaptive changes in response to those of the environment — genetic changes that occur during the evolution of the species, physiological and anatomical changes that occur during the existence of each particular organism. In higher species and especially in humankind, these biological mechanisms are supplemented by adaptive social forces. Early in the present century, however, the Harvard physiologist L.J. Henderson pointed out that there was more to fitness than the adaptive potentialities of living things. As he claimed in his famous essay "The Fitness of the Environment," the achievement of fitness depends not only on adaptive mechanisms but also on the fortunate fact that the terrestrial environment has certain physicochemical attributes which happen to be just right for life. But this theory now seems essentially meaningless for the following reasons.

Many present forms of life would certainly be annihilated if the surface of the Earth were very different from what it is now. They could not adapt rapidly enough if the salinity, the acidity, the relative proportions of gases, minerals and organic substances — or any of the other physicochemical characteristics of the Earth — were to deviate far from their present values for any length of time. In other words, the present environment does indeed exhibit fitness for the present forms of life but — and this is what Henderson had overlooked — it would have been unsuited to those of the distant past. An atmosphere with 21% oxygen, for example, would have been extremely toxic for the earliest forms of life.

During the past 3.5×10^9 years, the global environment has progressively changed, probably as a consequence of the activities of living things, and living things also have undergone corresponding changes through a feedback process. The Gaia system postulated by Lovelock

therefore seems to be a result of co-evolution. Instead of listing the chemical examples of this creative process discussed by Lovelock, I shall quote a picturesque phrase taken from one of his recent articles: "The air we breathe can be thought of as like the fur of a cat and the shell of a snail, not living but made by living cells so as to protect them against an unfavorable environment."

A few years ago, theoretical discussions were instigated by NASA to consider the possibility of making the planet Mars suitable for human life — which meant providing water, oxygen, moderate temperatures, protection from ultraviolet radiation, and so on. The general conclusion was that Mars could be made habitable only through the progressive introduction of living species capable of creating, over an immense period of time, more and more complex ecosystems similar to the ones which have evolved on Earth during more than 3×10^9 years. This analysis has helped us recognise the profound and innumerable changes that life had to bring about on the surface of primitive Earth to create, for present living things, the fitness of the terrestrial environment that L.J. Henderson had taken as the normal state of affairs.

According to the Gaia hypothesis, the Earth's biosphere, atmosphere, oceans and soil constitute a feedback or cybernetic system which seeks an optimal physical and chemical environment for life on this planet. At any given time, this system results in a relative constancy both in the composition of the environment and in the characteristics of living things. Repeatedly throughout his book, Lovelock refers to this equilibrium as "homeostasis" — a word invented by the Harvard physiologist, Walter B. Cannon, to denote the remarkable state of constancy in which living things can maintain themselves despite changes in their environment.

The word homeostasis, however, does not do full justice to the Gaia concept, which implies in addition that living things have profoundly transformed the surface of the Earth while themselves undergoing continuous changes, in a co-evolutionary process. Practically all the examples that Lovelock discusses refer, in fact, to creative evolution rather than to homeostatic reactions. For example, the accumulation of oxygen in the air which became significant 2×10^9 years ago (as a result of biological photosynthetic activities), probably destroyed many forms of life for which this gas was poisonous. In Lovelock's words, however, "Ingenuity triumphed and the danger was overcome, not in the human way by restoring the old order, but in the flexible Gaian way by adapting to change and converting a murderous intruder into a powerful friend." Cybernetic mechanisms progressively brought about the emergence of biological species capable of living in the presence of oxygen and of using it for the production of energy. In this case, as in

most other environmental changes, the Gaian way was not an automatic homeostatic reaction but a creative co-evolutionary response.

It seems worth considering that the Gaian control results in global homeostasis only over a period of time which is short on the evolutionary scale. One figure will suffice to illustrate the magnitude of the terrestrial changes that are continuously caused by life. In their aggregate, all the green plants now fix approximately 840×10^{12} kilowatt hours of solar energy per year in the form of biomass. This is more than 10 times the amount of energy that all of humankind uses annually, even with its most extravagant technologies. Who can doubt that this continuous process of accumulation of organic matter and energy will eventually affect both the surface of the Earth and various forms of life. Furthermore, Lovelock himself points out that the process of change may pick up speed and complexity as a result of human interventions, and he appropriately quotes me in stating that, on a local level, profound co-evolutionary changes have occurred in certain terrestrial

environments and in their biological systems during historical times.

In the last chapter of his book, Lovelock has the courage to explore the relevance of the Gaian hypothesis to the effects of human interventions into nature. I wish I had space to explain why I agree with him when he states that environmentalists often shoot at wrong targets because the resiliency of the Earth, considered as an organism, probably makes ecosystems more resistant to pollution than commonly believed. As I cannot discuss these problems here, I shall conclude by expressing my wish that in the next edition of his book, Lovelock emphasises not only the homeostatic aspects of the Gaia hypothesis but also its creative aspects. This would be in the spirit of his statement that the Gaia concept is an alternative to the "depressing picture of our planet as a demented spaceship, forever travelling, driverless and purposeless, around an inner circle of the sun". □

René Dubos is Professor Emeritus at the Rockefeller University, New York.

Pollution in perspective

Kenneth Mellanby

A Perspective of Environmental Pollution. By M. W. Holdgate. Pp. 278. (Cambridge University Press; London, New York and Melbourne, 1979.) £15.

SOME ten years ago I was invited by a British publisher to write a book with the title *Pollution in Perspective*. This was to have been a 'popular' book in which I would try to distinguish between real, damaging pollution and trivial environmental contamination which, though harmless, nevertheless caused so much public concern. Being an idle fellow I procrastinated, and my text is still mainly in my imagination. Therefore, when I saw Dr Martin Holdgate's new book, with so similar a title, my emotions were mixed. On the one hand I felt guilt for not having completed my own book on such an obviously important subject, and on the other hand I experienced relief that someone else had done the job so competently.

For there can be no doubt that Dr Holdgate has produced an excellent book. Although he modestly denies having given his subject complete coverage, I cannot find any significant gaps. All major topics in the field of pollution are dealt with

clearly, scientifically and with a full understanding of the facts, where these are easily available, and also the lacunae in our knowledge are always mentioned.

The book starts by placing pollution in its ecological context, and then goes on to define pollution and classify pollutants. A very important chapter is "The significance of pathways" which deals with the way substances are dispersed in the air, in fresh water and in the sea. The significance, sometimes overestimated, of the transmission of toxic substances through food chains is assessed. The great value of the book is that it constantly relates the concentrations of specific pollutants in the environment to the real effects on man or other targets. It thus shows how standards for pollution control may be scientifically determined, and how monitoring may be used to determine dangers and enforce controls. The costs of pollution control, and the way these may — or may not — be balanced against benefits are discussed. The international problems caused when pollutants cross frontiers are described.

The general theme is admirably stated in the book's last paragraph:

"Finally, there are grounds for optimism. There appears to be no reason why pollution should be the doom of mankind or the destroyer of the ecological balance of the world. But pollution control is an essential element in sound environmental management. The higher the standards of environmental quality and safety we demand, the more effort we shall have to make, and the more it will cost. It is a matter of wisdom and judgement how much risk is acceptable and how high environmental quality should

stand amid the other goals that compete for the resources of society".

No doubt there are those who will accuse Holdgate of "complacency" for not preaching doom and gloom, but thoughtful readers will welcome his clear assessment of the national and global situation. He shows that if mankind is destroyed by pollution, it will be our own fault.

Within its limits, which I shall discuss later, this book deserves nothing but praise. It is well written, and reasonably free from jargon. It will be a godsend to lecturers in universities, polytechnics and colleges of higher education who have to give courses on pollution or pollution control. Most of them could improve their current lectures simply by reading aloud from Holdgate's text.

My only criticism of the information given is that it is not always up to date. Dr Holdgate is a senior civil servant, with the characteristic respect for his sources, particularly where these are such things as the prestigious reports of the Royal Commission on Environmental Pollution. He reproduces (as others have done) a number of their admirable diagrams. For instance, from their first (1971) report we have graphs showing the amounts of smoke and sulphur dioxide in Britain's air at different dates. These figures show the remarkable improvement in air quality between 1950 and 1968 or 1969. For smoke, we are even given the "projection" for the year 1975, four years before this book appeared. As Dr Holdgate is Director General of Research in the Department of the Environment, where there are many junior scientists who have up-to-date figures for the period since the Royal Commission reported readily available, it is a pity that the diagrams were not redrawn and updated. This is not a trivial point, for the result would have reinforced many of the book's arguments, for the figures would have shown that there has been a further, substantial, improvement in air and water quality right up to the present day.

Notwithstanding this minor fault, this is a book which deserves a wide circulation. However, I fear that its sales will be reduced by the way it has been presented by the publishers, who have not served their author well. The text is set in reasonably clear type, but it is much too small to make reading a pleasure. The sections all bear unnecessary numbers (for example, 2.5.1 Pollution in the air) which may make prospective buyers who run through the pages in a book shop think that they are being offered a government report, and so they will be put off. Finally, the price of £15 for 278 pages (with no expensive plates) will not deter the lecturer who has to deliver a course on the subject, but his students will not be able to afford their own copies. This may, of course, be welcomed by some teachers, who will be able to keep up the pretence

that their oratory arises from their own original deliberations. The book is also too costly to circulate widely among concerned members of the public who need the information to allow them to make correct decisions on environmental problems. Also, though well written, the style is of the good scientific paper, which may present difficulties to those used to lighter literature.

So, although Dr Martin Holdgate's *A Perspective of Environmental Pollution* is a fine book, valuable to the élite, it may

not reach the mass audience envisaged by the publisher who wanted me to write *Pollution in Perspective*. So I fear that Dr Holdgate may not have let me off the hook, and that I may still have to write my own book. If I do, I, like all future writers on this topic, will have to thank him for marshalling so much information so admirably, and for reducing our work so considerably. □

Kenneth Mellanby is Editor of the international journal *Environmental Pollution*.

Pragmatic humanism

Stephen H. Schneider

The Climate Mandate. By W. Roberts and H. Lansford. Pp. 197. (Freeman: San Francisco and Reading, 1979.) Hardback £6.70; paperback £3.30.

IN the past five years at least twice this number of popular books on climate has crossed my desk. Some promise ice (for example, *The Cooling*), others fire (for example, *Hothouse Earth*) and one even has the title *Ice or Fire*? Among these offerings one of the most recent, *The Climate Mandate*, is one of the best. Its authors are Walter Orr Roberts, former Director of the National Center for Atmospheric Research (NCAR) and Henry Lansford, a science writer and former Information Officer at NCAR. Dr Roberts is presently Director of the Program in Food, Climate and the World's Future of the Aspen Institute for Humanistic Studies. His concerns with humanity are well reflected in *The Climate Mandate*.

The team of a scientist/humanist and a science-writer has resulted in a very readable (and mercifully short — only 197 pages) selection of topics related to climate and climatic change. We are spared the uncaveated railings and pet theories of some climatic prognosticators that climatic doom is nigh as well as the bland assurance of some ostrich-like professional meteorologists that there is no climate problem worthy of public note, let alone a dozen books.

Of course, in 197 pages one cannot fully lay out the range and depth of all phases of the climate problem. *The Climate Mandate* will thus likely be only a partial help to those looking for a non-specialist textbook on climatic change to supplement, say, a beginning level college course in geography. On the other hand, it is much better than most of its competitors in

confronting directly the place of climate and climatic variability in the world food picture. In fact, the book is organised to build up to the last chapter ('Defining the Problem — Malthusian Pessimists, Social Idealists, and Technological Optimists') in which the authors offer scenarios for world development within the demanding constraints of population growth, environmental stress, ideological differences, economic inequities and, of course, fluctuating climate. The scenarios comprise 'the climate mandate'.

To back up their solutions to the world predicament, there are chapters which review briefly climate history; the physical factors influencing climate; the climate theories of various scientists; the difficulties of climate forecasting; the respective roles of climate; technologies and infrastructure in crop productivity; and a cautious description of some weather modification operations in the US. If one extrapolates slightly from their carefully hedged remarks on weather modification, they seem to suggest that more dollars have flowed from granting agencies to weather modifiers than from seeded clouds to water users. They caution that such technological fixes are not panaceas, an apt thought in which to transition to the final chapter, where the food/population/energy/environment/climate problem (that is, the human predicament) is addressed.

The human predicament had been addressed often in the two hundred years since Malthus, and Roberts and Lansford bring it up to date with an overview of three modern contrasting views. First, there are the 'Malthusian pessimists', personified by ecologist Garrett Hardin, who counsel 'lifeboat ethics', whereby rich countries like the US are advised to abandon hope of feeding chronically poor countries with high population growth rates. The 'technological optimists', on the other hand, believe that modern energy and capital-intensive farming can easily accommodate the foreseeable growth of world population — if only Third World governments would provide markets for farmers to sell their produce and incentives for corporations to transfer their

technologies. Finally there are the 'social idealists', who fear that transfer to the poor of modern large-scale technologies is another form of imperialism, as it makes the developing countries dependent on products developed and produced abroad. They counsel the overthrow of the 'élites' who dominate Third World governments and the establishment of locally self-reliant, labour-intensive production systems.

Roberts and Lansford believe, as do I, that it is simplistic to view the human predicament simply as a problem of monolithic cause ('the danger lies in the conviction that a single aspect of the problem is so overriding that attempts to deal with any others are simply a waste of time and money'). They propose, instead, an approach they call 'pragmatic humanism', in which we are to accept the 'premise that many human lives can be saved and much misery avoided by a diversity of efforts'. Technology or the Green Revolution are legitimate tools in this 'whole-system approach', but their applications must meet local needs. The authors then offer 'scenarios' which comprise 'the climate mandate'. The first element is to establish a 'world food emergency reserve' and distribution system to mitigate the effects of local climatic variability. (This reviewer could hardly disagree without revoking his own writings.) Next is the need to develop agricultural self-reliance in developing nations — with US and USSR joint-help. The key to success is flexibility and cooperation on all sides. Specific examples of how to bring this about, however, are few. According to their scenarios the Earth could 'have the ability to produce adequate food for a doubled or tripled world population', but they admit (and unfortunately this is the only reference to this crucial issue) that 'the ecological implications have not been examined in any comprehensive way'.

The authors conclude optimistically, despite the litany of obstacles they properly point out, that 'if we heed the climate mandate, and if we accept the fact that the Earth's people are bound together by mutual needs and expectations that must transcend our rivalries and contests, humanity should be able not only to survive but to prevail over the hunger and starvation that have threatened so many people for so many centuries.'

The Climate Mandate is a compassionate book; it reflects the authors' own humanity. Its hopes and sentiments are appealing. But if past experiences with global cooperation remain our only reference, I would continue to rate the prospects as 'technologically optimistic, but politically bleak'. □

Stephen H. Schneider is a climatologist at the National Center for Atmospheric Research, Boulder, Colorado, and Editor of the journal *Climate Change*.

Nuclear detective story

J.H. Fremlin

Nuclear Disaster in the Urals. By Zhores A. Medvedev. Pp.214. (W.W. Norton: New York; Angus and Robertson: London, 1979.) \$12.95; £5.95.

DR MEDVEDEV has spent much time in studying widespread but indirect information about a very serious nuclear accident which occurred in the Urals, seemingly around 1957. His book begins with an extensive account of the hard and ingenious detective work which was needed to extract information from seemingly irrelevant papers on radioecology published in Russia, often years after the event. He gives an impressive picture both of the all-pervasive thoroughness of the censorship and at the same time of the number of points which nevertheless slipped through, and from which he has built up a convincing picture of serious contamination over a large area on the eastern side of the southern Urals where the original Soviet military nuclear industry was situated.

Dr Medvedev seems unnecessarily anxious to establish his excellent case for the reality of the disaster, and his arguments are not always individually convincing. For example, he says that papers written during the following few years on the radioecology of the region purported to describe the take-up of radioactive material, especially ^{90}Sr (strontium-90), by plants and animals and the food chains connecting these. To do this properly, he claims that less than 10% of the animals concerned could have been trapped or shot without disturbing the ecology which it was desired to investigate. This is hardly relevant, at least in the short term, for deer which are at the end of a chain (assuming that human hunters are not to be sampled). Using this figure of 10%, he deduces that the area contaminated must have been at least ten times the area found by dividing the number of deer shot, by the average population density. It could however, have been intended to shoot 100% of the larger contaminated ungulates, to prevent them from migrating to regions where they might later be shot and eaten. In this case one would deduce a maximum area ten-times-smaller than Medvedev does.

The book has clearly been written rather hurriedly, leading to some errors. For example, on page 173, he states that β -particles can penetrate 2 — 8 cm into living tissue and he (or the translator) has missed a misprint of protons for photons.

More seriously, on page 74, he defines the permissible dose of radiation as being the amount that is assumed not to cause harmful effects, and on page 21 says that the next generation will suffer severely if they are born from parents with ^{90}Sr in their bones. This and its daughter product ^{90}Y (yttrium-90) are both pure β -emitters with a range of only a few millimetres in tissue.

In spite of these minor errors, I accept without reservation that a major accident must have happened around 1957 which contaminated probably tens and conceivably hundreds of square kilometres — to a level of 1000–4000 Ci/km². For the reason given above, I do not accept the numerical estimate of 400 square kilometres of heavy contamination, but there seems no doubt that Dr Medvedev is right in describing the event as a major disaster, and that this was connected, like our Windscale reactor fire, with the military production of plutonium for bombs.

The final sixth of the book is speculative. The censorship has successfully hidden the cause of contamination. The US intelligence services may know the truth, but the thoroughly "sanitised" documents extracted from the CIA do not divulge it. Accordingly Dr Medvedev has had to rely on hearsay. Early guesses by local but uninformed people included an accidental bomb explosion and an escape of material from a runaway reactor. A third guess is that the wastes left after extraction of plutonium and unsatisfactorily stored, exploded. At first sight either of the first two seems possible and the third seems impossible on thermodynamic grounds, for the same reason that you cannot make a good fire with the ashes of an earlier one. Nevertheless, this is the theory that Medvedev espouses, and as his arguments are plausible they need to be examined.

The major positive argument is the size of the area affected. In each square kilometre the ^{90}Sr observed was of the order of that produced by the fission of a kilogram of uranium or plutonium. By 1957 the accumulated wastes could have sufficed to cover 400 km² if an adequate distribution mechanism existed. So could a 'dirty' H-bomb, with no distribution problem; but a fire in a runaway reactor could hardly do so. The actual area covered by heavy contamination is therefore important.

The second argument is the low ratio of ^{137}Cs to ^{90}Sr which varied from 1:8 (in a lake) to 1:1000 in soil, instead of the roughly 1:1 expected from fission. Dr Medvedev suggests that most of the ^{137}Cs had been removed from the wastes for industrial or medical use. The large difference between lake and surface soil, however, looks much more like the result of leaching away of the mobile caesium in the soil leaving the less mobile strontium near the surface.

The chief argument against the waste-explosion theory is the impossibility of producing an explosion which would pulverise the (non-volatile) material to the 1–10 μm sized particles needed to spread it over hundreds of square kilometres. Such an explosion would have to be of the same order as the Bikini H-bomb test and is not consistent with the type of steam explosion that could arise due to water running into radioactively heated waste. This could throw a lot of material for hundreds of metres but could not produce the fine pulverisation of the whole mass of material needed for its uniform distribution.

Dr Medvedev's alternative source of energy lies in the plutonium with which the wastes are invariably contaminated. At the Hanford works in Richland, Washington (one of the largest atomic plants in the US) some 100 kg of plutonium was concentrated over a decade, by a process equivalent to chromatography, in the topmost layer of mud in the trenches into which liquid wastes were run. This process might indeed eventually produce a critical concentration and this could support a chain reaction. This would, however, necessarily start slowly with a "delayed-critical" concentration in wet material, as the plutonium could not be chromatographically concentrated in the dry. This reaction would probably raise the temperature and reduce reactivity to equilibrium values at which plutonium was burnt as fast as it was added. At most it could raise the temperature only so fast (the delayed doubling time being several seconds) as again to produce a steam explosion. It is difficult to see how this could reach the effect of even a ton of TNT and quite impossible to see how it could reach the megaton scale required to contaminate hundreds of square kilometres.

Although the visible flash lighting up the sky reported by the CIA in 1955 (page 195) is consistent with an accidental H-bomb explosion, I do not think this the only possible explanation of the facts. I am unconvinced by Dr Medvedev's ecological arguments that the area involved was 400 km², and a very respectable smaller area could have been contaminated to the level observed by an uncontrolled reactor fire in which a large part of the uranium fuel was burnt and dispersed with the smoke of burning carbon moderator. Dr Medvedev realises himself that there are difficulties with any of the mechanisms proposed for a waste explosion. In his own words (page 163), "Truly, scientific imagination (or a capacity for 'science fiction' if you will) is needed to construct hypotheses about the exact causes of the explosion". I can only agree. But I hope a lot of people will read the book and see whether they agree too. (I congratulate the translator.) □

J.H. Fremlin is Professor of Applied Radioactivity at the University of Birmingham, UK.

Unorthodox epidemiology

D.A.J. Tyrrell

Diseases from Space. By Fred Hoyle and Chandra Wickramasinghe. Pp.196. (Dent: London, 1979.) £6.95.

THIS is an unusual book. It is well produced and easy to read, being written in a narrative and popular style; but its six chapters and three appendices are apparently intended to be a serious presentation of a theory put forward by the authors. The subject matter ranges widely. They start with cosmology and their interest in the organic molecules to be found in interstellar space. They suggest that life may have evolved in cometary bodies composed of organic chemicals, which would have had an inner zone protected from radiation and warmed to about 10°C by internal chemical reactions. In this "pool", primitive life-forms like bacteria and viruses evolved and then, when the comet passed near the Earth, were shed into space as micrometeorites, protected from ultraviolet radiation by a coating and sufficiently small not to be overheated on entering the Earth's atmosphere. They then sank towards the Earth, were carried on down to its surface by storms, and thus initiated biological life in the primeval Earth. They further assert that the process continues and that clouds of viruses, particularly those of influenza and the common cold, rain down upon the Earth and cause epidemics of these diseases; and that epidemics of smallpox, and of bacterial diseases like cholera and plague, may occur in the same way.

The authors have obviously read widely and thought deeply, and I am unable to express a useful opinion on their theory of the origin of life. However, as they extend the theory to explain epidemics, this can be examined in relation to present knowledge of infectious diseases. For instance, they argue that influenza viruses descend from space and are breathed in by birds, animals and man, and that the transmission from person to person or animal to animal is unimportant. They do not explain how an organism which must have produced untold billions of particles in a cometary puddle in space (and which they suggest may have arrived on Earth inside a bacterium) was also exquisitely adapted to replicate in avian and mammalian cells. The influenza virus has specific functioning elements by which it penetrates membranes, involves the cell nucleus, is replicated in ribosomes and forms new particles by inserting viral protein into the cell membrane which then bulges out and envelopes the virus nucleic acid and other peptides lying in the cytoplasm beneath. In Earth laboratories many common cold

viruses, rhinoviruses and coronaviruses multiply only in human cells, and only some such cells — in what sort of cells do they replicate in space? The influenza viruses found around 1930 have almost exactly the same internal peptides as those that circulate now — does all influenza come from one cloud of meteorites?

A key fact of their argument is that they have looked at published literature, investigated outbreaks of influenza in schools and found no evidence that influenza spreads from person to person. They state that if influenza did spread in this way it would be distributed in the children in a school by a random process. They show that it is not random — at Eton some houses were heavily affected and others virtually free, as judged by clinical diagnosis — so they prefer the earlier theory that influenza is due to a "miasma". It is stimulating to have current thinking challenged in this way, but I doubt if their theory provides a better model to explain known facts than do our present concepts. There is evidence that different

individuals shed varying amounts of virus, so in small groups they would be expected to infect at different rates — and I think the spread of the recent H1N1 virus from China across the USSR, and to Hong Kong and across the world, is better explained by spread from person to person than by viruses descending from space first in one area and then in the next. I would expect an influenza virus coming from space to appear over a very wide area if it really has to sediment slowly and negotiate the jet streams as the authors describe, even if it does survive desiccation and ultraviolet radiation.

I cannot agree with the theme of the book, which smacks more of science fiction than of science, but I think it is good that it has appeared. I would hate to think that unorthodox views could be suppressed, or that authors could never be published if editors or reviewers did not like their work. □

D.A.J. Tyrrell is Deputy-Director and Head of the Division of Communicable Diseases at the Clinical Research Centre, Harrow, UK.

US politics and the test ban

Edward Bullard

Blowing on the Wind: The Nuclear Test Ban Debate, 1954-60. By Robert A. Devine. (Clarendon/Oxford University Press: New York and Oxford, 1978.) £7.95.

THIS book is a detailed account of the reactions of US politicians, scientists and the public to the attempts to stop tests of nuclear weapons. It is confined almost entirely to the time when Eisenhower was President (1952-60) and is a political and sociological study rather than a technical discussion. Technical questions are mostly dismissed with the statement that some scientists said one thing and others said the opposite.

To have the events, and the views of the people concerned, set out in chronological order is useful. There are some well-documented judgements that run counter to widely held beliefs; for example John Foster Dulles appears as a strong and consistent supporter of a test-ban.

Useful as it may be, the book makes dull reading. This is, in part, due to the almost exclusive concentration on US views; negotiations require at least two parties and the interest lies largely in the contrast of aims and methods of the two sides. The

extent to which this book ignores all non-US participation is lamentable. The only references in the bibliography to publications by non-American authors are to Khrushchev's memoirs (transcribed and edited in the US), *Sakharov Speaks* (also a US publication) and Harold Macmillan's memoirs. The last of these is the only item in the bibliography that is not published in the US. It is, of course, difficult to understand the motivations and internal struggles of a closed society, such as the USSR; it is, however, important to make the effort. The first route to understanding is the study of official pronouncements and propaganda. If propaganda loses touch with the real world and with real intentions, it loses plausibility and becomes unconvincing to those it is intended to influence or deceive. For example, it was possible to follow the German retreat across Russia in 1944 by noting the westward progression of the locations of alleged German victories. For the Russian views on the test ban there is much more evidence than propaganda.

The 1958 'expert' discussions hold a special place as the first discussions with the Russians in which there was any real meeting of minds. Stalin had been dead for 5 years and Khrushchev had consolidated his power. There was a new situation in which Russian good faith and intentions had to be assessed anew. These matters are inadequately dealt with by the author who seems to have read only the final agreed report and not the transcripts of the day by day discussions, which are much more instructive.

The 1958 meetings were also of interest from another point of view. The American delegation consisted of a mixture of Hawks

and Doves who had not reached agreement on a 'party line' before setting out for Geneva. The reason for this probably lay in Eisenhower's belief in consensus and dislike of controversy and of having to decide between contesting parties. The meetings of the western delegates were often difficult. Most of those present were interested in assessing Russian intentions and motives, but the Hawks were primarily concerned to prevent any kind of agreement with the USSR. They even maintained, for a while, that atmospheric tests could not be sufficiently monitored because the wind might blow round and round in circles and never carry the radioactive debris out of Russia. By confining himself to published sources and Presidential papers the author has missed the details of these interesting controversies. He seems not to have discussed the negotiations with any of the participants.

The breakdown of the negotiations for a complete test-ban came in the political talks late in 1958. The US withdrew its support for the conclusions of the 'experts' concerning underground tests, introduced hastily analysed data from recent tests and declared that the technical matters must be discussed *de novo*. This interesting situation is very inadequately discussed and no references are given to Russian views; for example, to the detailed discussions by Riznichenko.

Throughout the book the discussion of technical matters is marred by an apparent lack of interest in the meaning of numbers. For example, on page 103 it is stated that Willard Libby calculated the amount of Sr-90 in the atmosphere to be 24 megatons. It is doubtful if every reader will understand this oracular statement. Much more confusing are the two values given for the amount of Sr-90 in the soil of the US in 1958 (pages 263 and 272); these differ by a factor of a million. The larger of them is a factor of 1000 less than that given by the AEC for 1961 in *Effects of Nuclear Weapons*. This muddle may be connected with the author's belief that m is the abbreviation for micro.

Perhaps I have been unduly severe, the book is about American politics and my complaints are that it is not about other aspects of the subject. It does unearth some fascinating things, such as a remark made in 1958 by a member of the President's Scientific Advisory Committee. He (who was he?) is said to have said: "These men who don't want a test moratorium are like a kid you are trying to put to bed. First he wants a drink of water and then he wants to go to the bathroom, but what he really wants is not to go to bed". □

Sir Edward Bullard is an Emeritus Professor of Geophysics of the University of Cambridge, UK, and of the University of California at San Diego. He attended the 1958 Geneva discussions on the possibility of a test-ban treaty.

Commitment to logic

Aaron Novick

Origins of Molecular Biology: A Tribute to Jacques Monod. Edited By A. Lwoff and A. Ullmann. Pp.246. (Academic: New York and London, 1979). \$17.50; £11.35.

MOLECULAR BIOLOGY had its origins in several centres which served as gathering places for people from around the world. In the very beginning, it was Cold Spring Harbor in New York and soon after the Institut Pasteur in Paris and the MRC Laboratory in Cambridge, among others. These places developed for a variety of reasons not the least important of which was the presence of some of the leading figures in this new field. At the Institut Pasteur it was André Lwoff, Jacques Monod and Francois Jacob. Jacques Monod died in 1976 and a number of his colleagues and disciples have contributed to this *Tribute*, a volume which describes from a number of points of view an exceptional person who played one of the major roles in the development of our present understanding of the control of gene expression. From its title, it seems to be a companion volume to *Phage and the Origins of Molecular Biology*, edited by J. Cairns, G.S. Stent and J.D. Watson (Cold Spring Harbour Laboratory, 1966), a volume dedicated to Max Delbruck on his sixtieth birthday.

The personal accounts in volumes such as these provide descriptions of important and fascinating details in the development of scientific ideas never reported in the usual forms of publication. Because of its memorial character, the present volume includes many personal details in its descriptions of a man of great spirit whose life outside the lab as well as in it was of heroic scale, whose friends included scientists and public figures throughout the world.

Of particular interest is the collection of personal statements from most of the people involved in the series of discoveries which culminated in the giant step represented by the Jacob-Monod model for gene expression and regulation. The reports provide a fine illustration of the development of a great scientific idea, but one must recognise that the picture is limited by the modesty of some of the participants in this memorial volume. André Lwoff and Francois Jacob were no less important both to the exciting and creative spirit at the Pasteur and for their own remarkable scientific contributions. As a history, the volume does not make it adequately clear that the critical experiments which showed that control of the *Lac* gene occurs through action of an endogenous repressor could be done only

because of Jacob's timely development of the necessary genetic technology.

It is also fascinating to follow the development of Monod as a scientist. Here is a man for whom science was a great personal adventure and a means of personal expression, yet a man fervently dedicated to logic and reason. He exulted in the power of deduction and was known to shout after an observation verified one of his deductions that this was again proof that Descartes was right and Kant wrong. Despite his commitment to logic, he had a remarkably successful intuition for how things must be, and he could present these pictures with great force. Even when he was later proved wrong, the vehemence and sharpness of his argument expedited the clarification of a problem.

Some of the authors also note his audacity. He never limited himself to the disciplines of his education nor did he ever restrict himself to minor objectives. In his crowning work, the development of the allosteric model for regulatory proteins, despite being trained as a zoologist he used modern physical chemical ideas with no inhibitions to formulate a remarkably original and innovative theory. "It is no longer a question of right or wrong", one of my colleagues in the field remarked. "The Monod theory has changed the style of thinking among the biochemists."

An impressive feature of the volume is the honesty of some of the reports which describe the personal faults as well as the greatness of Monod. His enthusiasm and pursuit of fundamental problems inspired the people he worked with. His candour came as an exciting surprise when it was first encountered by his disciples. This lack of stuffiness along with his generosity and the confidence he placed in his students created love and great loyalty. But he also had personal faults, and these too are reported. He could be vain and arrogant in a pointless way. Surely it is because they held him in such high regard that his colleagues were free to describe these faults so honestly.

As occasional allusions in the volume indicate, Monod's life outside of science was also remarkable. He was aware, wise and, when he felt it necessary, active in the world of politics. During the hysteria in the United States in the early 1950s, when foreign visitors were required to sign non-communist affidavits, the *Bulletin of the Atomic Scientists* published statements by a number of European scientists; I recall that by far the best of these was the one by Monod, who with characteristic perception saw the larger implications of US policy. Again, on the occasion of the Nobel Prize, rather than basking in the adoration and pride the French have for their Nobel Prize winners, he took advantage of the public attention to improve the support of science in France by making a strong public statement severely critical of his government's science policy,

a statement which apparently infuriated DeGaulle.

Some contributors make reference to Monod's service during World War II in the Resistance and later in the re-established French Army, but the volume's guidelines prevented fuller description of these parts of his life, for the same reasons the authors say little about Monod's significance as a public philosopher, illustrated by his book, *Chance and Necessity*, which was a sensational bestseller in France.

The essays are generally of exceptionally high quality, and they will bring back memories of great times for the large number of scientists throughout the world who have spent time with Jacques Monod and his colleagues in those laboratories

built originally for Louis Pasteur. It will also bring the pleasure of enlightenment to many others who were not directly involved. In addition, for those totally outside of molecular biology, it is a worthy addition to the developing literature on the origins of this field which has so revolutionised biology. And this appearance of a memorial volume ought to stimulate interest in a more complete biography of this impressive man whose life touched so many of the important developments of the middle decades of this century. □

Aaron Novick is Professor at the Institute of Molecular Biology at the University of Oregon. He spent 1953-54, 1962-63 and 1967-68 in Jacob and Monod's laboratories.

Challenge to promissory materialism

Anthony Flew

The Human Mystery. By John C. Eccles. Pp. 255. (Springer International: Berlin, Heidelberg and New York, 1979.) DM34.

EVEN had Sir John Eccles not begun this his own first series of Gifford Lectures with quotations from "My great master, Sherrington" (page 2) any sympathetic reviewer would have been bound to refer to the fitting facts that it was just 40 years earlier, under the same foundation and in the same University of Edinburgh, that that "great master" himself gave the lectures which were later to become *Man on His Nature* (Cambridge, 1940). *The Human Mystery*, though thoroughly worthwhile, lacks the magic of that predecessor: how could it not? The present Eccles project, of which we have here only the first and probably less distinctive half, is strictly in accordance within the terms of Lord Gifford's will: "... to promote and diffuse the study of Natural Theology in the widest sense of that term — in other words the knowledge of God".

The aim is to mount a challenge to what, following his friend Sir Karl Popper, he calls "promissory materialism", a challenge along the entire front but with the main weight concentrated in the sector of his own lifelong concentration, the human brain. Promissory materialism is defined as the "claim that science is so powerful and pervasive that in the not too distant future it will provide an explanation in principle of all phenomena in the world of nature including man, even human consciousness in all its manifestations" (page 7). So, after a first

introductory lecture, Eccles proceeds through the "Origin and Evolution of the Universe", the "Planetary System and Planet Earth", the "Origin of Life and Biological Evolution", to "Human Evolution: The Story of Cerebral Development". It is in the second half that we come to the real speciality of the house: "Cultural Evolution with Language and Values: The Human Person"; "The Creation of a Self"; "Structure of the Neocortex: Conscious Perception"; "Learning and Memory"; and "The Mind-Brain Problem".

To the scientific layman the story which Eccles tells in his first half is fascinating, though here and elsewhere to follow him closely requires frequent consultation of those handy Penguin dictionaries of the sciences: if he has succeeded in his attempt "to present scientific material . . . with a minimum of technicality", then one must pray to be spared the failures.

The Gifford aspect appears at once in "the Big Bang story as suggesting the operation of a supernatural Creator" (page 15); although it is curious that Eccles mentions only in an aside the notion of a Creator upon whom — whether or not, He, or She, 'in the beginning' also started the Universe off — it continues to be always absolutely dependent. After all, it was precisely and only continuous creation in this theological sense which St Thomas insisted could be known on the basis of natural reason, without benefit of revelation.

Two other Gifford points stressed in the first half are the unpredictable chanciness of the emergence of life, and of the actual course of biological evolution; and the fact that the whole cosmological story would have had to be very much as it has been if beings capable of knowing that story were going to become part of it. About the former Eccles maintains, and surely he is right, that "There is no predictable line of evolutionary development" (page 49). It seems to be as true of the evolutionary biologist as of the human historian that most of his most

important explanations are of how something was possible, rather than of why it was inevitable. No doubt other readers will share my own pleasure in two pieces of Eccles mischief: the suggestions that the most primitive mammals "brought about the dinosaurs' downfall by preying on their eggs" (page 58); and — of "the attempt to communicate with super-intelligent humanoids in our galactic system" — that it is "highly likely that this romantic project will be killed by boredom" (page 73).

In wondering what to make of the second of the two points stressed in the first half we must give some weight to the point, which Eccles does not notice, that these conclusions are derived only for a Universe obeying the same fundamental laws of nature. The argument is that "If we economise and have the Big Bang producing the mass for one galaxy of 10^{11} stars, which is still an immense universe", then, given what we now know of the fundamental laws of the actual Universe, "the time from Big Bang to Big Crunch is reduced to one year" (page 28). But a Creator, having it in mind to furnish his creation with potential knowers, would not, presumably, be restricted either to or by any actual or possible natural laws.

In his rather longer second half Eccles is at least equally fascinating. In lecture 6 he begins by contending, as is surely correct, that "cultural evolution is exclusively human" (page 98). This and much of the later discussion is presented in terms of Popper's distinction between "three Worlds: World 1, the matter-energy of the cosmos; World 2 of all subjective experiences; and World 3, which is the cultural heritage of mankind" (page 98). The reader needs to be aware always, as their spokespersons so often are not, that the second and third of these can be identified only as aspects of the first. We have, that is to say, no knowledge of any kind of consciousness other than the consciousness of organisms; and perhaps we cannot even give sense to talk of any consciousness that is not thus rooted in the matter-energy of World 1. The whole cultural achievement of World 3 is likewise embodied in, and inseparable from, such incontestably World 1 objects as buildings, books and computer tapes.

In the rest of this lecture Eccles considers the enormous importance of language and — what could not exist without language — the self-consciousness which is so much more than mere consciousness. As one expression of his constant and most welcome concern to resist the 1984 which is "engulfing more and more of our planet" (page 237), and after crediting to the Sumerians the two incomparably important inventions of both writing and the wheel, Eccles remarks that for most of its history Sumer "was an amazingly open and tolerant society" (page 114); though it does not occur to him that those market

interests which he was earlier inclined to chide might have been one necessary condition of this tolerance (page 110).

Lecture 7 examines "the role of World 3 in producing the next generation"; making much, but never too much, of the crucial fact that it is thanks to this that "The creation of a cultured person" can now "be accomplished in a few years", whereas "it took at least 50,000 years to create a high civilisation" (page 123). This chapter contains one section which will especially delight any philosopher who has ever faulted Hume's *Treatise of Human Nature* for its "paralytic's eye view of causation": Eccles tells of experiments with kittens in gondolas which show that exploratory learning will not take place without active movements by the learner (page 132).

Lecture 8 on "Conscious Perception" constitutes necessary preparation. In lecture 9 on "Learning and Memory" the thesis is that memory is essential to anything deserving to be called knowledge: "Without memory there could not be a knowing of existence" (page 180). In lecture 10 Eccles wants to construe mind and brain as "independent entities, the brain being in World 1 and the mind in World 2 (Fig. 6-1)", and to urge that these are both entities which "somehow interact, as illustrated by the arrows in Figure 10-2" (page 212).

But this, as the rally-drivers say, is going a bit quick. For all our ordinary talk about minds, ordinarily understood, is just talk about certain sorts of things which some creatures of flesh and blood can and do do or suffer. To say that, for instance, she has a first-class mind just is to say that she is capable of operating at that high academic level. So if anyone wants to hypothesise some independent entities to be called minds, he has first to provide some account of how such entities are to be identified and individuated. For minds in the common everyday sense of the word are not what is required: they are not, that is to say (logical) substances — things which, like chairs and tables and unlike grins and tempers, could significantly be said to exist separately and in their own right. To speak of her first-class mind surviving her death and cremation would, in the everyday sense of 'mind', be about as sensible as speaking of the grin on the face of Alice's Cheshire Cat outlasting the cat of whose face it was a configuration. On the other hand, much of the history of philosophy since Descartes can be read as showing how difficult if not impossible it must be to think up a notion of minds as immaterial substances; which could be identified as subjects of discourse, re-identified through time, and individuated one from another. □

Antony Flew is Professor of Philosophy at the University of Reading, UK.

Precious cult of scientific knowledge

Martin Pollock

Paradoxes of Progress. By Gunther S. Stent. Pp. 231. (Freeman: San Francisco and Reading, UK, 1978). Hardback £8; paperback £3.90.

THIS is a collection of articles on modern science, already published over the past ten years or so and now strung together, a little forcedly perhaps, under a title which can serve a multitude of themes. It is therefore, inevitably, somewhat of a ramble. The common thread is Professor Stent's own idea of what is happening to our precious cult of scientific knowledge, where it is going and what its principles mean, or should mean, for us. His opinions are worth studying, though cramped by a rather awkward style of writing and even if — or especially if — one does not agree with them. The problems he raises and the questions he asks are those which most scientists do not even like to think about, let alone try to answer.

All the essays are worth reading in their own right, although two of them — a review of Jim Watson's *Double Helix* and an analysis of "Prematurity and Uniqueness in Scientific Discovery" — stand rather apart from the rest, being of borderline relevance to the central issue. Three are of outstanding interest. These are: (1) "The Dilemma of Science and Morals" which discusses the many desperate problems of how our continuously expanding knowledge should be applied practically and includes a brief but fascinating comparison between the science and technology of classical China and western scientific philosophy; (2) "Limits to the Scientific Understanding of Man", being essentially a clear-cut criticism of positivism and its later manifestations in the form of simplistic acceptance of a reality that is "built on cumulative experience" alone and is now referred to as "Scientism"; and (3) "The Decadence of Scientism" ('Decline' might have been a more appropriate word), which discusses a neo-Kantian basis for understanding and a practical morality that recognises the impossibility of true objectivity or value-free conclusions, and involves adopting what is now often referred to as a "Structuralist" and anti-behaviourist approach to thinking and acting; this itself depends on analysis of "deep structures" beneath the superficialities to which alone our senses are directly responsive.

According to Stent, science, as we now know it, is on the way out. The spirit of "Faustian man" who believes in

"progress" and outward striving (defined as the "will to power") is on the wane and yielding diminishing returns; it is anyway self-limiting because it seeks, and to a large extent obtains, a sense of security which quenches the thrust for more power. Faustian man, born in the ages of enlightenment of the seventeenth and eighteenth centuries and reaching maturity in the nineteenth where the solution to all problems was viewed in the context of a continuously progressive increase in knowledge and power over the outside world, is on his death bed. His spirit will be succeeded by something similar to the Polynesian-based dream of a life of ease but without grand ambitions, a rejection of the idea of "progress" and materialistic sophistications and an acceptance of the Zen principle that the recognition of subjective sensation is the only reality. The "noble savage" is not a fancy directed backwards to the distant past, but something to anticipate in the years to come. The different articles share a common theme by illustrating the problems and paradoxes which herald the end of our era. And the author, who has rightly emphasised the many analogies between science and the arts, believes that similar factors are involved in the decline of the arts which have now lost all style and discipline, become totally "freed" and will have to start again with a new impulse.

One of the first signs of the end was, according to Stent, the "beatnik" movement in Berkeley of the late 1950s and (to a later and lesser extent) the hippy creed of the 1960s. Amongst scientists themselves, the relevant factors include a growing sense of the limitations to the objectivity of our observations and conclusions and increasing estrangement between our intuitive common sense and what we have to accept as most appropriate explanations; in particular, the principle of indeterminism in physics, which is equivalent to saying that like causes do not necessarily have like effect would seem to undermine the fundamentals of scientific explanation.

Stent also refers to a phenomenon described by Mandelbrot termed "second-stage indeterminism" where probably random events, such as "noise" in an organised system, theoretically able to be eliminated by a statistical approach, nevertheless seem on analysis for limited periods, to conform to certain laws of fluctuation (for example, in coin tossing experiments). This problem is the old one of how to decide when to introduce the concept of chance and what the idea of randomness really means — a dilemma which has faced scientists for very many years. To what extent, for instance, are the structural patterns we think we see around us simply illusions, based on too superficial and prematurely completed analysis of a series of events that require an impractically long period of study for

establishing their truly random nature?

One might go further on the basis of belief in subjective reality, and ask, even in the name of science, how many of the patterns we think exist in nature are only a reflection of pre-determined patterns in our brains. But we would still have to try and decide how our brain patterns appeared in the first instance.

Associated with the rather difficult idea of "second-stage indeterminism" is that of the "spontaneous activity of the system itself" which Stent also pursues. This is really rather frightening. Are we to suppose that every system in nature has some inherently endowed freedom of action which transcends natural laws and is thus immune to scientific study? If so, it might still be argued by Mandelbrot (if not by Stent) that this is no more than what most people ascribe to the human organism in the form of intrinsic freewill, upon which we all base our ordinary lives (and our science) whether we believe in it or not. And so we pass on to the equally difficult concept of *self* and one's own consciousness, forever a stumbling block for most philosophers. Even the most positive of positivists would surely have to admit that to use the machine itself for studying the machine is begging a shattering question and must involve some crucial assumptions, such as that the "thing in itself" is "truly" (whatever that may mean) what we perceive it to be, which few of us would be prepared to accept.

The final paradoxical problem raised concerns the moral dilemma of what should be the principles guiding our actions in science. And it looks here rather as if Stent is more than just vaguely sympathetic to the Taoism of ancient China which teaches that man is part of an inscrutable nature and must retreat from personal striving in order to attain inner fulfilment. This, of course, is the direct opposite of Western science where nature is *not* regarded as "inscrutable", but on the contrary responds strikingly to reason and has allowed us to exploit our environment with extravagant success — at least viewed from a strictly technological angle. With Tao, "instead of Truth and Justice", he writes, "Wisdom and Harmony would [then] become the primary values". And he quotes Joseph Needham: "with their appreciation of the relativism and subtlety and immensity of the universe, [the Chinese scientists] were groping after an Einsteinian world picture without having laid the foundations for a Newtonian one". Is the implication here that, in one sense at least, the Chinese have leap-frogged Western science and could soon be way ahead on the basis of a Tao-based structure for dealing with ourselves and the world around us?

Some recent advances in brain physiology are then described, in particular the fascinating work of Hubel and Wiesel on cells of the visual cortex. This emphasises the specific selective nature of

Sorry, for copyright reasons some images on this page may not be available online

cell response to visual stimuli, indicating that patterns we "see" are made up of an integrated synthesis of the reactions of a composite of cells programmed by the combined effect of early environment and genetic predisposition to respond only to certain restricted types of input signal. This kind of selective mechanism of response to the immediate environment applies also to other types of (biochemical) cell reaction, such as enzyme induction. It is another aspect of the type of evidence that supports a "structuralist" approach to the mechanism of understanding, being closely related to Chomsky's ideas of "deep structures" in linguistics and has taken over, during the past 30 years or so, according to Stent, from the later stages of positivism expressed, for example, in "behaviourism" which is now largely discredited. And so, it is argued, we are back — or nearly so — to the original ideas of Kant in favour of "innate, *a priori* knowledge" (that is, *not* derived from experience) which could have evolved. Darwinistically, because it was the most suitable for survival at the time. And why not? If we cannot achieve absolute understanding, why not make do with the brain mechanism presumably evolved to supply the type of "explanation" most suitable for dealing with ourselves in the world as it is — or as it was!

Stent seems inclined to use a similar neo-Kantian method for postulating an "innate ethical deep structure", present in all

human beings, which he recognises as not all that far removed from Kant's "categorical imperative", defined as an ethical principle so universally applicable that it has to be accepted as a natural law . . . so obvious that it "goes without saying" — and thereby, one suspects, is different for every individual because nobody ever seems to have to formulate it in words.

One does not have to accept all or any of the implications offered in this book in order to benefit from thinking about them. The author is not very dogmatic, anyway, and only in his predictions about the end of our era in science does he attempt to make a firm case — which is, in fact, not very convincing. We may, perhaps be at a point of inflection in the development of science, but does it really amount to the end of an era? It is indeed, strange to view his arguments about the forthcoming "age of leisure" and a rejection of material efficiency, against a background of a world where nearly 50% of the population exist near or below subsistence level and the simplest types of technological improvement could, if properly applied, ease the lot of hundreds of millions of human beings. Modern science may not reveal the truth about the Universe or solve our ethical problems, but so long as people want H-bombs, space exploration, computer technology, and so on, or simply fast transport and more plentiful forms of energy and food; then our science will be needed because it alone can deliver the goods. A philosophy of pragmatism still has a lot to be said for it, but it is not much discussed here, except as a rather unimpressive spin-off of what the author dismisses as "soft-core" scientism — a less noxious type of scientism in comparison with the "hard-core" variety which maintains that science (especially biology) provides a morality (a "moral norm") of its own based on evolution and the "natural behaviour" of animals.

This is a stimulating and thought-provoking book which is worth reading in depth by all scientists who want to consider seriously the meaning of what they are doing and who wonder why they are sometimes pressed to discuss the philosophical implications of their work and not restrict themselves to its immediate practical results or just fiddle around with an intellectually amusing toy. Our science would be in a better position to defend itself if there were more scientists who can react to Professor Stent's arguments and at least understand what it is *not*; and who can realise, with A.N. Whitehead, that despite (or along with) all its practical achievements and intellectual magnificence, we are liable "to forget how strained and paradoxical is the view of nature which it [modern science] imposes on our thoughts". □

Martin Pollock is Emeritus Professor of Biology in the University of Edinburgh, UK.

Exercises in the traditional style

John Ziman

Teleology Revisited. By Ernest Nagel. Pp. 352. (Columbia University Press: New York and Guildford, UK, 1979.) \$25.

THE official theology of science — as it might be enacted for example by the Council of the Royal Society if they were so wrongheaded as to ignore their own statutes forbidding such exercises — is empirical rationalism. For several centuries philosophers have been trying to elucidate and validate this creed. Of course, like any successful cultural movement, science really justifies itself by its works. But there is a species of intellectual who is not satisfied with the appearances of power, and tries to draw back the curtain hiding the machinery of science and show that it really does deserve our confidence.

In the past twenty years or so, these philosophers at the court of science have suffered a rude shock: all that they could find behind the fearful mask of the Wonderful Wizard was a little old man, gentle and wise but with no hot line to the Absolute. Critics such as Karl Popper, Norwood Russell Hanson and Thomas Kuhn have effectively demolished the claims of the scientific method as a means of arriving at certain truth.

For the older generation, this movement of Reformation has been an unhappy experience. Should they trendily embrace the latest doctrines, or should they stick with familiar beliefs that they cannot honestly discard? Professor Nagel retains "the outlook of an unreconstructed empirical rationalist", which he defends with characteristic wisdom and tolerant precision of thought and expression in this collection of essays. Although these were published independently over a period of more than 40 years, and are not artfully melded into a continuous narrative, they are remarkably consistent and coherent in style and content. If their outlook would be stigmatised as old-fashioned by the Younger Turks, it is not reactionary, and is very far from outmoded as a practical faith for the working scientist.

In fact, there are truths here that must be reckoned with. In the earlier chapters he brings to a halt the sloppier elements in Popper's fallibilist attacks on the traditional position. It may not be possible to define a general distinction between theory statements and observation statements, so that all science is in principle conjecture. But that does not mean that scientists are

talking nonsense when they make such distinctions in the course of their research. Nagel acknowledges Popper's contributions in other respects, but repulses what he aptly calls the "Mephistophelian view of science . . . according to which to suppose even for a moment that any problem is really solved is to lose one's soul". And he annihilates Paul Feyerabend's irregulars after their wildly undisciplined charge to the cry "anything goes".

On the other flank, he repudiates false allies. The critique of Carnap's attempt to construct a logic of inductive reasoning is polite and detailed — but devastating. The mathematical theory of statistical inference has, I think, made some technical progress in recent years, but no intellectual structure can be safely founded on a symbol that is supposed to stand for the number of primitive predicates that might hypothetically be postulated concerning some body of evidence. To put it more succinctly than Nagel, it all seems to be a question of knowing how many beans make five. Empirical facts do not support theories by any device of strict logic.

Nevertheless, within these limits, his position is very open to attack from quite another quarter. That is to say, his genuine concern for the realities of the research process is applied solely to the arguments by which scientific knowledge is justified in the public literature. He admits that "assured knowledge in science is the product of a community of thinkers, each of whom is required by the tacit traditions of his group to be unsparing in his criticisms and evaluations of the cognitive claims presented to him" (page 13). But he does not seem to realise the corollary — that the scientific community may be (usually quite reasonably) persuaded to accept a cognitive claim on evidence that is much less watertight logically than philosophers would like. Nagel quite ignores the element of what Michael Polanyi called "tacit knowledge" in the assessment of research, and makes no reference to the social relations of the scientific community where this non-logical expertise is valued and shared.

In this light, the earliest essays in this book (dating from the 1930s) are of peculiar interest and significance. They show in detail, through the history of algebra and geometry, the pressure that can be exerted on an empirical science by the demand for logical consistency and completeness. The paradoxical appearance of imaginary numbers and imaginary points gradually drove nineteenth-century mathematicians into the modern stance, where each branch of pure mathematics is regarded simply as a system of relations derived conventionally from a prescribed set of axioms, without reference to any particular reality. In every stage of this process, extra power is gained by the increased generality of the results; but the

outcome can only be correctly stated in Bertrand Russell's dictum that the pure mathematician does not know what he is talking about nor whether what he says is true.

Empirical rationalists have always been strong supporters of mathematical theory in science. They are very conscious of the value of reliably rigorous logical passages in scientific statements. But the more we purify a mathematical formalism, the more we come to realise that it is only the *medium* of communication between scientists and does not of itself constitute a *message* about the natural world. The empirical element in a scientific statement can only be expressed intelligibly in natural language, whose categories are inevitably somewhat vague. It is a pity that Nagel's remarks on this point were written before Stephan Korner had demonstrated its deadly significance for any strong logic of scientific justification.

What is also missing is a realisation of the dependence of scientific communication on non-logical human capabilities such as pattern recognition. It is true that a geometrical theorem can only be proved generally by the juxtaposition of abstract symbols for logical relations: but for most practical purposes the old Euclidean method, with its reference to diagrams, is sufficiently convincing. From experimental high energy physics to sociobiology, every branch of the natural sciences is knit together by communications conveying diagrammatic inferences that cannot be interpreted by any known logical formalism but which are perfectly intelligible to another human being.

In the real world, it is the consensus that can eventually be reached by systematic intersubjective communications that defines our standards of objectivity and rationality. This applies at every level, from the everyday world of tables and chairs to the hidden world of quarks and neutrinos. It also applies to metascientific discourse on such questions as the relationship between theory and observation, or between cause and function. The point is that words like these are thematic rather than categorical. Like a picture, or a diagram, or a familiar model, they can convey very important ideas which cannot be defined, or paraphrased briefly, or precisely, or entirely unambiguously. They can only be understood in the light of experience, not of formal logic. In the final essay, Professor Nagel struggles to define the concept of teleological explication in biology, and effectively admits at the end that it was an impossible task.

Nevertheless, such strenuous exercises in the traditional style remain highly instructive for the research scientist, who must surely continue to believe, along with Professor Nagel, that "the logical methods of the modern natural sciences are the most effective instruments men have yet devised for acquiring reliable knowledge of the world and for distinguishing warranted

claims to such knowledge from those that are not". This (as the Council of the Royal Society would correctly perceive) is the faith upon which science is built, and the disciplinary code, at platoon, regimental, and divisional level, which binds it together in its war on ignorance and error. And yet

there are perhaps occasions when such simple loyalties fail us, and the direction of the Army itself has to be called into question. □

John Ziman is Professor of Physics at the University of Bristol, UK.

Updated science policy almanac

Austen Albu

Science and Government Report International Almanac, 1978-1979. Edited by D.S. Greenberg and A.D. Norman. Pp. 368. (Science and Government Report, Inc., P.O. Box 6226, 3736 Kanawha St NW, Washington DC, 20015, 1979.) \$54.

It can be assumed that any study published today on government policy and organisation for science will be more concerned with technology than with pure science. Whether in capitalist or communist countries this represents a victory for those pre-War marxist scientists who advocated planned support for science applied to utilitarian ends. The new edition of this valuable report, covering a period when economic difficulties restrained the expenditure of most countries on R&D, makes it clear that pure science plays a decreasing role in government support policies compared with applied science and technology. Even Israel, which claims high support for basic research, based on its traditional approach to learning, has seen a significant increase in the proportion of applied research and development in the past few years. Although they do not all follow the same pattern, these national reports give an invaluable picture of recent developments in public policy and attitudes, and in changes in organisation for scientific advice and the carrying out of policy.

All governments support R&D, but the degree to which they do so financially and the organisations they use for the purpose vary a good deal. Britain and France seem to be among those countries with the most centralised structures among the advanced industrial nations. Even the USSR, if one forgets the overarching position of the Party, seems to have a wider range of institutions, although they are constantly changing. The growing emphasis on R&D to improve industrial production seems to have led to some decline in the prestige of the Academy of Sciences in face of the State Committee for Science and Technology.

In the United States the growth of anxiety in official circles about the country's apparent diminishing capacity for industrial innovation was one reason for President Carter's proposals to raise the rate of growth of funds for R&D, especially basic research. Congress, however, had rather different ideas and kept the 1979 expenditure to a total only fractionally more than that of 1978. One of the results of the increased involvement of governments in science and technology is the politicising of the decision-making process. In that most democratic of federations, Switzerland, the voters in referenda have displayed hostility to expansion of the universities and to subsidies to industry for R&D. This may be of little importance as Switzerland has the highest per capita rate of R&D expenditure in the world; 80% of it by private industry. Apart from wishing to curtail government expenditure, some voters in most countries are becoming increasingly interested in 'ethical' aspects of science or questions of the effects of technology on 'life style'. The main targets at present are nuclear energy and recombinant DNA. The former is an obvious embarrassment for governments struggling with energy problems and no doubt adds to the growing part energy plays in national research programmes. Popular interest in the supposed dangers of recombinant DNA has been greatest in the USA and UK; in most other countries it has only attracted the attention of scientists and administrators.

The richer countries are concerned with problems of health research, both its changing nature and its accelerating cost. In the USA the Secretary of the Department of Health, Education and Welfare addressed scientists last year on the need to devise "health research principles" to be used for planning a "rolling" five year budget for the Department's programmes. The Federal Republic of Germany has published a programme of Promoting Research in the Service of Health, 1978-1981, of which an extremely interesting excerpt from the English translation is reproduced. It includes an examination of the difficulties of health research and a detailed list of fields in which greater R&D efforts would seem to be necessary.

So far the Trades Union in most countries have not shown much sustained interest in the problems involved in the results of scientific research. Only in the Scandinavian countries have permanent bodies been established by the Unions to

keep them under survey. In France the scientific associations acted as pressure groups during the Presidential election of 1979 in which science policy played a prominent part.

Some rather unexpected figures in the output of scientist are revealed. In Sweden there was a fall in the output of Doctorates in the Natural Sciences between 1970 and 1976 from 461 to 172. In Britain, during the period of university growth in the 1960s scientific subjects got left behind, so that the "swing away from science" in the 1970's seems by contrast fairly modest. On the other hand engineering, at least in numbers, kept pace with university expansion. This, however, does not take account of a rapidly growing number of foreign students. The most unbalanced figures come from India which, in 1977, produced 140,600 graduates in the Natural Sciences and 15,000 in Engineering; bringing the total number of science graduates in the population to 1,182,272 of whom 16.1% were unemployed and of engineers to 251,860 of whom 2.4% were unemployed.

The most significant differences between nations lie in the ratio of government to private industry financed R&D and the proportion of military expenditure. This may provide at least a partial explanation for the decline of British industrial performance. In Britain, France and the USA government provides more than half the nation's R&D funds; in Germany, Italy, the Netherlands, Sweden and Canada between 40 and 50%. In Japan the figure is about 30%, but Japan has the third largest R&D programme in the world. What is more significant is the fact that in the UK and the USA roughly 50% of government R&D funds are spent on military programmes against a EEC average of 23%, a German figure of 12 and Japanese of 2. In all the major Western countries except the UK the share of government R&D spent on military programmes declined during the 1970s. In the UK it increased between 1970 and 1976 from 41 to 48%. If research expenditure is to be reduced these figures indicate where the possibilities of cuts should at least be scrutinised. On the other hand it seems that R&D activity by industry has been declining in the UK while that of the UK's main competitors has been rising; a matter which must be of concern to a government committed to reversing the decline of British industrial competitiveness.

This is the second year of publication of this important almanac. As an essential source of reference for scientific administrators, politicians and students of the subject it is to be hoped that it has now become firmly established in the rather overgrown forest of journals dealing with science policy. □

Austen Albu is a Visiting Research Fellow of the Science Policy Research Unit, University of Sussex, Brighton, UK.

New myths for old

Jon Beckwith

From Genesis to Genocide: The Meaning of Human Nature and the Power of Behavior Control. By S.L. Chorover. Pp. 238. (MIT Press: Cambridge, Massachusetts, and London, 1979.) £9.35; \$14.

In recent years a number of controversies have erupted over theories and practice in the biological and medical sciences. These debates include the subjects of genetics, race and IQ; the XYY male; sociobiology; psychosurgery; behavioural control practices in prisons; and the giving of drugs to school children said to be suffering from minimal brain dysfunction. A number of books have already appeared which deal with most of these issues from a critical perspective, including notably Kamin's *The Science and Politics of IQ* (Halsted: New York, 1974), Schrag and Divoky's *The Myth of the Hyperactive Child* (Dell: New York, 1975) and Ann Arbor Science for the People's *Biology as a Social Weapon* (Burgess: Minneapolis, 1977). However, nowhere, to my knowledge, has there been any extensive attempt to draw connections between all of these controversies. Now, Stephan Chorover, in this remarkably concise piece of writing (208 pages of text), for the first time, places all of these issues in a common framework and describes them in terms of a long historical tradition which preceded them.

Chorover, a psychologist at MIT, with a long-standing interest in abuses in psychology and psychiatry, unites what might seem to be disparate subjects by analysing them in terms of "meaning and power" in the realm of behaviour control. By these terms he refers on the one hand, to those mythologies, religious doctrines or scientific theories, which have served to structure people's view of their place in the world. "... what people believe about the essential nature of human beings has a powerful influence upon social expectations. Such beliefs tend to shape the ways in which people in a given social context are treated, and these in turn, significantly influence how they behave." Thus, "... ideas about human nature ... deserve to be regarded as powerful instruments of behaviour control in their own right". "Power", on the other hand, refers to the power of certain groups in a society to apply these theories in practical ways for social control. The extreme example is, of course, genocide practiced by the Nazis based on biological theories of racial inferiority and superiority.

The book abounds with other historical

and contemporary examples. Perhaps two of these will give some feeling for the analysis. In 1851, Dr Samuel Cartwright, a respected Louisiana physician, published a report commissioned by the Louisiana Medical Association purporting to explain among other things why there were runaway slaves. The roots of this problem, according to the doctor, lay in a disease of the mind which he termed "drapetomania", "the insane desire to wander away from home". Various punishments of the runaway slave could then be considered merely as medical treatments.

In a contemporary case study, Chorover describes in detail the story of "Thomas R." a portion of whose brain was removed during the heyday of psychosurgery in the late 1960s. Among other frightening stories associated with this case, he reports that the surgeons concluded that Thomas R. was psychotic partly on the basis that he was convinced that his wife was "carrying on with a neighbour". However, after the surgery took place his wife filed for divorce and eventually married that same neighbour. Thomas R., himself, has been socially non-functional since the operation and has spent much of his time in mental institutions.

Chorover, in reviewing the long history of what are essentially biological determinist theories, goes back to what he refers to as "Plato's lie". This term refers to the theory presented in *The Republic* that different people are born with different qualities of metals (gold, silver or brass and iron) mingled into their bodies, and that the metals in turn determine what status in society individuals will occupy. According to Plato (through Socrates) such a lie is necessary to justify existing social stratification. To Chorover "the basic texture of human nature mythology remains everywhere and always the same and ... Plato's myth of the metals may be considered a prototype for today's myths".

It must be asked, of course, whether modern science has provided a much more solid basis for theories of human nature than earlier religions and mythologies. Chorover's answer is a clear no. He points to arguments used in the nineteenth and early twentieth centuries in the name of science (eugenics, phrenology, craniology, and so on) which we now recognise as totally without foundation. As a curious means of self-justification in the face of their critics, practitioners of these sciences have always likened themselves to Galileo, persecuted for trying to present the truth. Of course, Galileo, as Chorover points out, was attacked because his theories challenged the established order of things, whereas the makers of what Chorover generally calls sociobiological theories have, for the most part, provided rationales for existing social arrangements. He sees contemporary sociobiological theories as having no more solid scientific

new books from
Blackwell

The Restoration of Land the Ecology and Reclamation of Derelict and Degraded Land

Studies in Ecology Volume 6 by A. D. Bradshaw and M. J. Chadwick. December 1979. 314 pages, 193 illustrations. About £12.50

This book deals with the problems of derelict land on a world-wide scale. It shows how the problems can be solved most effectively by a proper scientific understanding of the ecological factors that effect plant growth, but it takes a practical viewpoint and will be invaluable for the engineer and landscape architect as well as for the scientist.

Developmental Biology of Prokaryotes

Studies in Microbiology Volume 1, edited by M. Parish. 1979. 310 pages, 93 illustrations. £19.00

Prokaryotes are bacterial and related organisms. Their developmental biology comprises morphogenesis, differentiation and pattern formation or development. The book discusses these processes with reference to the bacterial cell cycle, sporulation, morphogenesis in arthrobacters, life cycles of streptomycetes, bdellovibrios, cyanobacteria and myxobacteria.

Plant Health the Scientific Basis for Administrative Control of Plant Diseases and Pests

Edited by D. L. Ebbels and J. E. King. December 1979. 334 pages, 21 illustrations. About £16.00

Population Dynamics

20th Symposium of the British Ecological Society, edited by R. M. Anderson, B.D. Turner and L.R. Taylor. December 1979. 448 pages, 144 illustrations. £20.00

Decomposition in Terrestrial Environments

Studies in Ecology Volume 5 by M. J. Swift, O. W. Heal and J. M. Anderson. 1979. 392 pages, 112 illustrations. £22.50

Demography and Evolution in Plant Populations

Botanical Monographs Volume 15, edited by O. T. Solbrig. December 1979. 240 pages, 36 illustrations. About £15.00

Blackwell Scientific Publications
Oxford London Edinburgh Melbourne

Circle No. 56 on Reader Enquiry Card.

From Churchill Livingstone

Biology of Senescence

Alex Comfort

1979 Third edition 414 pages
illustrated hardback £13.00

The only comprehensive work on mechanisms of ageing in man and other organisms.

Recent Advances in Infection—1

Edited by D. S. Reeves and
A. M. Geddes

1979 226 pages illustrated
hardback £11.00

First in a new series of up-to-date accounts of advances made in non-viral infections and clinical microbiology. Fourteen articles cover a wide variety of topics, written by experts in the field.

Annual Research Reviews

—provide detailed, comprehensive and critical reviews of all the work in a given field published in a particular year.

Brain: Hormones and Aggression Vol 2 £12.75
Carmichael: Adrenal Medulla Vol 1 £12.75

Forsling: Anti-diuretic Hormone Vol 3 £16.50

Oparil: Renin Vol 3 £20.25

Wallach: Proteins of Animal Cell Plasma Membranes Vol 2 £17.75

Horrobin: Prolactin Vol 6 £10.25

Hume: Biofeedback Therapy Vol 2 £6.50

Panayi: Rheumatoid Arthritis and Related Conditions Vol 3 £14.00

Taylor: Hodgkin's Disease and the Lymphomas Vol 3 £16.50

Lamberts: Physiological and Pathological Aspects of Prolactin Secretion Vol 1 £10.25

**Churchill
Livingstone**



Robert Stevenson House,
1-3 Baxter's Place, Leith Walk,
Edinburgh EH1 3AF

basis then their predecessors and laments the "inability or unwillingness of scientists to examine the social preconceptions inherent in the organization and conduct of their own work."

Although Chorover has done an impressive job of drawing the connections between his different topics, there are times when the attempt to unite all of the issues seems strained, as represented, for instance, by the title of one chapter "Genocide: The Apotheosis of Behavior Control". Further, although the role of sociobiological theories in justifying an inferior status for women is mentioned at several points, this subject deserves much

more extensive treatment, particularly in the light of the recent resurgence of such ideas. These defects, however, do not seriously detract from the unusual service that this well-documented and well-referenced book performs for biologists, social scientists, psychologists and the public at large. For, to this reader, one is not equipped to evaluate these issues as they appear without an analysis which considers the social context and historical background to particular questions at the interface of science and society. □

Jon Beckwith is Professor of Microbiology and Molecular Genetics at Harvard Medical School, Boston, Massachusetts.

Instantaneous expertise

Thomas H. Jukes

Malignant Neglect. By the Environmental Defense Fund and Robert H. Boyle. Pp275. (Alfred A. Knopf: New York, 1979.) \$10.

THE dust-jacket of this book modestly states that it "is based upon the enormous resources and scientific knowledge and authority of the Environmental Defense Fund (EDF), the nation's leading force in the field of environmental health". One author is a journalist, one a biochemist, one a science associate, and the qualifications of the other four are not listed.

A normal metabolite, acetaldehyde, is called a "known or suspected carcinogen" (page 105), and ammonia a "toxic organic vapor". The familiar litany is recited that no level of a carcinogen is insignificant, and that the latent period for development of cancer is 5-40 years (page 6). Actually, the risk and length of time required for appearance of symptoms are both dose-related.

A graph (page 21) compares increase in cancer mortality rate for 1940-1975 (uncorrected for smoking, page 214) with increases in production of plastics and other organic chemicals. Compared with plastics, similar increases have occurred in skateboards, tomato production and pocket calculators.

Chapter 3 is about polychlorobiphenyls (PCBs). There is no lack of public information on this topic. But what is the record of the EDF on PCBs? Jensen's publication in 1966 (page 64) attracted wide attention to contamination by PCBs. The EDF virtually ignored PCBs and campaigned against DDT, so that in 1969, the "end of the ocean" by 1979 was predicted as a result of the arrest of photosynthesis in marine algae by DDT. However, Harvey *et al.* in 1973 reported

that PCBs were present in surface water of the North Atlantic Ocean at about 20 p.p.10¹², and the level of DDT was less than 1 p.p.10¹². Scott found in 1975 that DDT, 100 p.p.m. of diet, had no effect on hatchability and shell thickness in laying hens, as compared with lethal effects produced by PCBs at 20 p.p.m. PCBs were dumped promiscuously, because they were never subjected to the justifiably careful regulations that govern insecticides.

Page 102: "Driving through New Jersey... On U.S. 1, ... one begins to detect a pungent odor, like that of rotting fruit. At first the odor is faint, but as the car swings into the New Jersey Turnpike, the smell grows stronger... Closing the windows does no good; the stench pours through the vents. The sky become visibly darker, like the twilight or an eclipse of the sun. At last, ... the source comes into view. It is perhaps the largest complex of oil refineries and petrochemical plants in existence... At night the flares atop the refineries produce an eerie light that transforms the scene into something from Dante's *Inferno*... Fourteen thousand people die each year from cancer in New Jersey".

On September 24, 1979, I drove south from Newark on the New Jersey Turnpike. I passed through the "refinery complex" at 6.45 p.m. There was no odour, there were no flares, and the only visible emission from the refinery was a few wisps of steam. To the west, there was a brilliantly clear sunset in which a range of hills, 30 miles away, was sharply etched against the sky.

Alarming statements are made about diethylstilboestrol (DES) used in meat production, and it is said (pages 149-151 and 219) to be detected in 1-2% of table meat and in pancreas. It has been detected only in liver, and only 0.6% of 8,293 beef livers sampled contained more than 0.5 p.p.b. The DES intake from meat is less than 0.001% of the equivalent daily oestrogen production by a nubile woman. Page 151 infers erroneously that nitrofurans are antibiotics, and states "Even minute residues of antibiotics in meat and poultry can sensitize people and cause allergic reactions, such as rashes and shock, when one of these antibiotics is medically administered". I know of no evidence for this. Insufficient emphasis is given to the carcinogenic role of alcohol.

Arsenic and chromium, listed as

carcinogens, are nutritionally essential trace minerals, which is not mentioned. Either there is a threshold below which such substances are not carcinogenic, or there is no threshold, and therefore life is carcinogenic, but we cannot deny *both* of these possibilities. But the authors repeatedly emphasise that there is no safe dose of any carcinogen, and, on page 211, they say "'Life' is not carcinogenic". I disagree. First, there must be a threshold for certain carcinogenic stimuli (such as iodine deficiency in rats). Second, life can be carcinogenic because mutations accumulate in DNA during ageing, including mistakes in DNA replication and those caused by environmental mutagens.

Appendix A says that caffeine "may cause miscarriages or birth defects". Such a statement is pointless without being quantitative and is also irresponsible and sensational. The final chapter is "The Solution to the Problem", emphasising pages 224-232) "Personal Involvement in the Regulatory Process".

Leading experts in the field of environmental cancer are far less dogmatic than are the EDF sextet. John Higginson concludes (*Science*, 205, 1363; 1979), that the manner in which people live — diets, dress, sexual and child bearing patterns, and especially tobacco and alcohol consumption — account for the great variations in cancer rates in different countries, and may be far more important than chemical pollutants. He reports that cancer patterns within Europe show no correlations with industrialisation. He says... "people would love to be able to prove that cancer is due to pollution or the general environment. It would be so easy to be able to say let us regulate everything to zero exposure and we have no more cancer. The concept is so beautiful that it will overwhelm a mass of facts to the contrary". □

Thomas H. Jukes is a Professor in Residence in the Department of Biophysics and Medical Physics, and a Lecturer in Nutritional Sciences at the University of California at Berkeley.

Potency of interferon

D. C. Burke

The Interferon System. By W. E. Stewart. Pp.421. (Springer: Wien and New York, 1979.) DM98; \$53.90.

THIS book is a comprehensive review of the entire interferon literature, and fills a considerable gap. The last single-author book on interferon appeared in 1969 and the last multi-author book in 1973. Since then a number of specialist reviews have appeared, but no-one until now has had the courage and energy to tackle a survey of the field single-handed. The author is to be congratulated on a fine achievement, and the book will be greatly used.

As the author points out, interferon has received considerable recent publicity in both the scientific and popular literature as a potentially useful antiviral and antitumour agent. Its potential as an antiviral agent has indeed been obvious ever since its discovery by Isaacs and Lindenmann in 1957, but it has been slow to realise it. In retrospect, this is partly because quite inadequate amounts of interferon were available for the early trials, and partly because we did not choose the most suitable infections for treatment.

Attention has now swung away from treatment of respiratory infections to such life threatening conditions as chronic active hepatitis and viral infections of immunosuppressed or immunodeficient patients. Here useful and encouraging trials are taking place. It is, however, the potential use of interferon as an anti-

tumour agent that has attracted most recent attention, for, stimulated by a careful ongoing trial against osteogenic sarcoma in Sweden, there have been several well-publicised reports of its activity against human cancer in the USA. In addition, interferon has emerged as a cellular modulatory factor, affecting the growth of cells, the immune system and the growth of tumours; and the mechanism by which it is produced is being investigated as a model for gene derepression in eukaryotes.

The book is therefore timely. Interferon research has continued apace and we greatly need a good critical summary. The book will be invaluable for those who are starting research in the area, but also for those who, like the reviewer, have been in the field a long time but who cannot remember who did what and when. The book has a complete coverage discussing topics as disparate as the structure of double-stranded RNAs, the genetics of the interferon system, the pharmacokinetics of interferon, and its role in normal recovery from virus infection, in addition to the trials as an antitumour and antiviral agent. The bibliography contains nearly 2500 references and the author has compiled 18 tables, many of which summarise information which has not previously been drawn together — for example, a compilation of the properties of type II interferon and a seven-page table of the cross-species activities of interferons.

However, the book is more than a compilation, for the author does not hesitate to comment, often constructively. There are, for example, interesting discussions of the different hypotheses which have been advanced to explain the mechanism of virus induction of interferon, of the mechanism of superinduction, and of the various schemes for interferon purification.

SCIENTIFIC BOOKSHOP

H. K. LEWIS can supply works in all branches of Pure and Applied Science. Catalogues on request. Please state interests.

SCIENTIFIC LENDING LIBRARY

Annual Subscription from £7.50. (Available in U.K. only)

Reduced rates for multiple subscriptions.

Prospectus post free on request.

Quarterly List of New Books and new editions added to the Library sent post free to subscribers regularly.

H. K. LEWIS & Co. Ltd.

136 GOWER STREET,
LONDON, WC1E 6BS

Telephone: 01-387 4282
Telegrams: "Publicavt",
London, WC1E 6BS."

Circle No. 59 on Reader Enquiry Card.

Bring Your Library
Up-to-Date With This
ANS Edition...

FERMI-1

NEW AGE FOR
NUCLEAR POWER

Historical Development Of
Nuclear Energy
In the United States

454 pages 6" x 9"
Hardbound ... \$27.80

American Nuclear Society
555 North Kensington Avenue
LaGrange Park, IL 60525 USA

Please take my order for _____ book(s).

Payment in full enclosed.
Bill me and I accept postage
and handling charges.

NAME _____

ORG. _____

STREET _____

CITY _____

STATE _____

Circle No. 58 on Reader Enquiry Card.

Unhappily, in spite of the wide usefulness the book will undoubtedly have, the book is flawed by personal animus against a few scientists, and by occasional lapses into slangy diction. Cells do not "quit" making interferon, and sentences like "Studies on the mechanisms controlling the transcription and translation of interferons will likely soon enable better artificial regulation of these

mechanisms, to provide sufficient interferon messenger RNA to allow its retrocopy into prokaryotic cells from which clones interferon can become truly abundant" make one gasp. □

D. C. Burke is Professor of Biological Sciences at the University of Warwick, Coventry, UK. He has worked on interferon since April, 1957, starting to collaborate with the late Dr Alick Isaacs and Professor Jean Lindenmann a month or two after the initial discovery.

Elements of cloning

Marie A. DiBerardino

Cloning: A Biologist Reports. By R.G. McKinnell. Pp. 130. (University of Minnesota Press: Minneapolis, 1979.) \$8.95.

PROFESSOR MCKINNELL terminates his book with the following three sentences in the epilogue: "Cloning is one of many experimental procedures that provide information that may help in solving problems such as cancer and ageing. That is the why of cloning. And to assist people in understanding that 'why — i.e., the rationale of cloning — I have written this book'. The author has accomplished his objective. He is a research biologist who has carried out nuclear transplantation studies (one form of cloning) directed towards understanding normal cell differentiation, cancer, immunobiology and ageing. Few scientists possess both the authoritative background and literary talent to communicate accurately the relevance of bench-work research to its future potential for solving biomedical problems. McKinnell, however, manages to convey the significance of this basic research to the non-scientist.

McKinnell begins his book by correcting erroneous and inflammatory statements about cloning and points out that the cloning of plants has been in practice for over 4000 years and has served to enrich man with beauty and food. This process is achieved by means of asexual reproduction resulting in a genetic replicate of the parent, whereas sexual reproduction involves the combination of genes from two parents and thus produces an individual containing a diversity of genetic traits.

The author then embarks on a description of classical animal studies carried out during the late nineteenth and early twentieth centuries that laid the ground-work for the amphibian cloning experiments. During this period there occurred a fusion of the disciplines of genetics, embryology and cytology; and the central problem that occupied these early scientists was the theory of nuclear

equivalence. They sought to determine whether the diverse specialised cells of an organism retain the same set of genes as the nucleus of the fertilised egg. The earliest scientists recognised the stability of the differentiated state, that is, liver remains liver even if a person lives beyond ninety years, as pointed out by McKinnell. To explain this phenomenon, a theory of genetic differences among the progeny of the zygote nucleus was proposed by Weismann to account for the origin of cell diversity and stability. However, this proposal was refuted at least for nuclei from the earliest stages of development by the primitive cloning experiments of Loeb in the sea urchin and later of Spemann in the salamander. Finally, in 1952 "a fantastical experiment" termed and proposed by Spemann, was accomplished by Briggs and King. They sought to extend the primitive cloning experiments and transplanted a living nucleus from a cell from a frog blastula embryo, a day old, into a frog egg whose own nucleus had been removed surgically. The blastula embryo contained thousands of cells all derived from a zygote nucleus, but these blastula nuclei were still capable of promoting eggs to develop into normal larvae and eventually in later studies into normal frogs, demonstrating that the donor nuclei contained a set of genes equivalent to the zygote nucleus. This prototype experiment has been repeated many times in various amphibian species throughout the world, and it is now well established that many nuclei from early embryonic stages are *totipotent*. The theory of nuclear equivalence is still the central problem of developmental genetics today. The cloning studies have been most extensively carried out in two amphibian forms — the leopard frog, *Rana pipiens*, and the South African frog, *Xenopus laevis*. Cloning experiments have shown that during the course of embryogenesis, transplanted nuclei become progressively restricted in their ability to promote normal development of the eggs; and so far no nucleus of an adult cell has programmed an egg to develop normally. Despite this, a most extraordinary result does occur when nuclei from adult cells are cloned. A small percentage of eggs develops through embryogenesis to early larval stages and contain all the cell types and tissues of a larva, indicating that an extensive gene complement is still present and functional. Similarly, frog nuclei from adult kidney

tumours when transplanted to eggs also lead to the formation of larvae. This subject, an area in which the author has made important research contributions, is discussed at some length. He points out that the formerly held pessimistic view of the irreversibility of cancer has been alleviated by these and other experiments. Thus, although important strides have been made in studying problems of normal cell differentiation and cancer, much more needs to be done in the future. McKinnell proposes: "If more were known about cancer-cell genetic material and about regulating its differentiated state, there would be the rational hope that a cancer chemotherapeutic agent could be devised that would regulate differentiation of these malignant cells".

Although amphibian cloning has been the most extensively studied among multicellular organisms, there has also been some work done on insects and fish. However, attempts at mammalian cloning have so far not been successful. But McKinnell points out that many of the techniques are available and the expectation that the remaining ones will be solved is encouraging. Cloning of farm animals may have agricultural advantages — for example, one could select for outstanding milk production, quality of wool, disease resistance, and so on; and this approach would be extremely faster than selective breeding for genetic traits.

Finally, McKinnell reviews some of the concepts of human cloning theorised by science-fiction writers, philosophers, theologians and lawyers. He addresses himself as a biologist and expert closer to the social, ethical and biological problems inherent in their suggestions. Among his various refutations he emphasises that cloning may result in genetic replicates but not carbon copies, a widely misunderstood point. He also points out that species are successful due to the diversity of genes available through sexual reproduction, and so cloning is not a sound reproductive method.

McKinnell has performed an important service for both scientists and non-scientists in his well balanced and critical review of cloning, and at an appropriate time when both groups need an accurate account of the applications of nuclear transplantation studies to the biomedical sciences, in order to evaluate the erroneous and exaggerated notions of cloning that have been perpetrated upon the public. This book will be especially invaluable to non-specialists. A series of superb illustrations, together with the clarity and simplicity of prose, will permit the non-specialist to understand the basic elements of cloning and its biomedical implications.

Marie A. DiBerardino is Professor of Anatomy at the Medical College of Pennsylvania, Philadelphia. Dr DiBerardino began her nuclear transplantation studies with the originators of cloning (Briggs and King) during the 1950s.

Cytogenetics stages its own revival

Susumu Ohno

Human and Mammalian Cytogenetics: An Historical Perspective. By T.C. Hsu. Pp. 186. (Springer: New York, Heidelberg and Berlin, 1979.) Paperback \$13.20; DM24.

IN 1959, Jerome Lejeune of Paris discovered the trisomy of chromosome 21 in those unfortunate individuals afflicted with the congenital syndrome then known as mongolian idiocy, now called Down's. With simultaneous discoveries by several British groups of the X0 sex chromosome constitution as the cause of Turner's syndrome in sterile women as well as of the XXY constitution in sterile men with Klinefelter's syndrome, 1959 heralded the birth of human cytogenetics. Although the scale was obviously at least an order of magnitude smaller than that of the discovery of the DNA double helix in 1953, these discoveries, nonetheless, generated immense interest. In the heady day of an emerging molecular biology that was sure to become the core of the new biology, who would have thought that the venerable chromosome cytology of a distinctively pre-War vintage would stage its own revival? Furthermore, in so delicate a creature as *Homo sapiens*, who would have thought so gross a genetic imbalance as the trisomy of a whole chromosome could give rise to live births?

In spite of its belated birth, at least by 10 years in my reckoning, the revived old soldier did not immediately fade away. On the contrary, subsequent events made a long success story out of human and attendant mammalian cytogenetics. Soon, Lyonisation (inactivation) of one of the female's two X-chromosomes was established as the dosage compensation mechanism unique to mammals, and the discovery of evolutionary conservation, as opposed to innovation, of mammalian linkage groups in general, and the X-linkage group in particular, dramatically altered our view of the nature of natural selection. Somatic genetics based on cell fusion to produce interspecific somatic cell hybrids became the precocious child of human and mammalian cytogenetics. The technique of *in situ* hybridisation proved useful in localising repeated DNA sequences on individual chromosomes. When an apparent senescence was about to start,

Caspersson came to the rescue with the innovation of a chromosome banding technique.

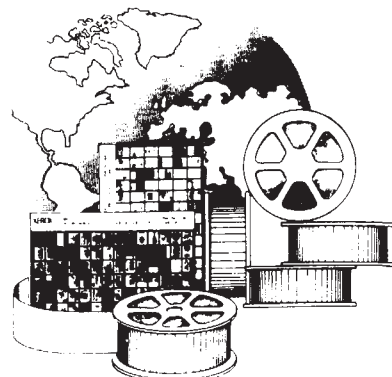
Now that senior members of the group involved in these initial excitements have passed or are approaching retirement age, one might expect a series of memoirs of those events. Professor T.C. Hsu of Houston opens up with a noteworthy salvo giving his own breezy and gossippy account. Of course, Rudolph Virchow's dictum *Omne cellule a cellule* applies equally well to scientific discoveries. The well publicised discoveries of 1959 were preceded by earlier ones; for example, the development of tissue culture techniques, the use of hypotonic pretreatments (T.C.'s own discovery) and colchicine, and the correct description of the normal human karyotype by J.H. Tijo and A. Levan that rectified earlier misunderstandings. Earlier still, a few outstanding investigators such as Sajiro Makino of Sapporo and Robert Matthey of Lausanne had accomplished a great deal in mammalian cytogenetics without any of the above noted modern conveniences. In T.C.'s portrayal of those participants of the drama, one finds a number of witty gems; for example his accounts of Sajiro Makino and Kurt Benirschke.

It should be pointed out, however, that three participants of the same event are likely to give three entirely different versions of it. The fact is that the excitement of 1959 was essentially a European affair to which those of us across the Atlantic played second fiddle. Therefore, I await with great anticipation equally witty, but entirely different versions from some senior members of the European group.

Who should read T.C.'s memoir? I should say everybody, particularly those researchers of the younger generation — as recommended by M.J.D. White in his foreword, but for a different reason. I see one lamentable defect in the otherwise bright young generation brought up with the television screen. Because of their apparent abhorrence of printed words, the papers that they never read are unashamedly quoted and misunderstood and the writing style of scientific manuscripts is becoming entirely monotonous, as though they had been turned out by the same old computer. Julius Caesar wrote his *Commentaries* and Augustus his *res gestae*. While nobody seems to care about them, almost everybody seems to know Claudius' gossippy memoir *a la* Robert Graves. If books like T.C.'s can rekindle the joy of reading in the heart of younger scientists, Professor Hsu should feel very proud. □

Susumu Ohno is Chairman of the Department of Biology at the City of Hope National Medical Center, Duarte, California.

This Publication . . .



is Available in MICROFORM

For Complete Information customers should write:

University Microfilms International

Dept. F A
300 North Zeeb Road
Ann Arbor, MI 48106
U.S.A.

Dept. F A
18 Bedford Row
London, WC1R 4EJ
England

Circle No. 72 on Reader Enquiry Card.

VOYAGER I

The 30 August issue of **Nature** contains 82 pages of results from Voyager's visit to Jupiter. For a copy write to: Macmillan Journals Ltd, Brunel Road, Houndsmills, Basingstoke, Hants RG21 2XS, UK.

Enclose a cheque made payable to Nature. Price per copy (post paid): UK £1.20; USA & Can. US \$3.50 (surface), US \$5.00 (air); Rest of World £1.50 (surface), £2.00 (air).

Circle No. 73 on Reader Enquiry Card.

Core of controversy over biohazards

Sheldon Krimsky

The Recombinant DNA Debate. Edited by D.A. Jackson and S.P. Stich. Pp.385. (Prentice-Hall International: Englewood Cliffs, New Jersey, and Hemel Hempstead, UK, 1979.) £14.55.

THE controversy of the past eight years over the regulation of recombinant DNA techniques has left in its wake some unusual and vexing policy issues. For the non-molecular biologist peering through the key-hole at the disputants, listening to a genetic vernacular that could pass as extra-terrestrial noise, the debate gives the appearance of a family feud. And it might have remained just that way were it not for the scientists who alerted the public to the potential hazards of their own work. Given the public's concern about this area of research and development, scientists may view similar acts of social responsibility as a danger to their disciplinary autonomy.

The principal target population affected by controls and regulation is a group of scientists engaged in basic research. Consequently, predominant expertise resides with a major interest group. The experts who are called upon to guide us through a safe technology path and on whom we must depend for objectivity can hardly qualify as impartial. Paradoxically, without them there could be no risk assessment.

The recombinant DNA episode holds many riches for science-watchers. It has stimulated discussion on a wide range of problems from public participation in the formation of science policy to the future prospects for human genetic engineering. In their edited volume *The Recombinant DNA Debate* David A. Jackson and Stephen P. Stich provide a series of essays that reach the central core of the scientific controversy over biohazards and, in addition, examine some of the moral and legal issues involved in the regulation of scientific inquiry. Stich, a philosopher, was on the faculty of the University of Michigan during the period the volume was in preparation. David Jackson, a University of Michigan microbiologist, was senior author of the first published paper on recombinant DNA techniques. Jackson also helped establish Genex, a US firm set up to develop commercial uses for recombinant DNA techniques.

The book, consisting of seventeen papers written between 1975 and 1977, is divided into three sections: Part I introduces the non-specialist to the

techniques of genetic engineering; Part II examines the risks and benefits from various sides of the controversy; and Part III considers legal, social and philosophical issues. Most of the scientific contributors have also been principal actors in the debate (A.M. Chakrabarty, Roy Curtiss III, Bernard D. Davis, Joshua Lederberg, Robert Sinsheimer and George Wald). For this review I shall limit my comments to selected essays.

A.M. Chakrabarty reviews the areas in which recombinant DNA techniques may prove fruitful. These include drug, chemical and fuel manufacturing, crop improvement, and the treatment of genetic disorders. It is too early to judge whether or not Chakrabarty's optimism that recombinant DNA, by revolutionising the manufacture of biologically active proteins, "would make them available in large quantities at modest cost and would contribute significantly to the betterment of human health and welfare." It is perhaps a symptom of the snail's pace of technology assessment that neither in this volume nor in the vast literature on this subject does their exist an analogous technical discussion of areas of potential misapplication or willful misuse of recombinant DNA technology.

Roy Curtiss III describes his construction of a strain of *E.coli* with twenty-four specific mutations designed to render it safe for molecular cloning. While initially an integral part of a strategy for biological containment, the skillfully engineered strain of *E.coli* (Chi 1776) may soon be irrelevant for the vast majority of experiments in the US. Recently, the Recombinant DNA Advisory Committee of the National Institutes of Health (NIH) voted to exempt most experiments from the NIH guidelines when ordinary laboratory strains of *E.coli* K12 are used. Little incentive remains for scientists to continue using the highly sensitive Curtiss strain despite its widely acclaimed safeguards.

Papers outlining the potential dangers of gene-splicing are contributed by Robert Sinsheimer, George Wald, and the recombinant DNA study group of Science for the People. Both Sinsheimer and Wald implore their colleagues to consider the long-term ecological consequences of this new-found power to rearrange genetic substance across widely divergent species. Their emphasis is on the possibility of unexpected events or "evolutionary booby-traps", in contrast to specific scenarios of danger.

As a counterpart to the DNA critics, there are contributions by Bernard D. Davis and Rolf Freter focusing on imagined, as opposed to real, dangers of the research. Davis invokes Darwinian evolutionary principles to argue that Nature abhors new pathogens. In his view, biological competition and natural selection operate in tandem to inhibit the establishment of novel pathogens in the

ecosystem. Freter reviews the experimental data relevant to the question of whether *E.coli* K12 can be transformed into an epidemic pathogen. The evidence, he concludes, suggests that we cannot produce an *E.coli* superpathogen by recombinant DNA techniques. Nevertheless, he emphasises the importance of weakened hosts in gene-splicing experiments for the safety of laboratory personnel and recommends the use of *E.coli* strains incapable of growing in germ-free mice (a property of Chi 1776).

Two philosophical papers appear in Section III. Stephen Stich examines several types of moral reasoning voiced during the most active period of the debate. He challenges the view that scientific research should be curtailed if it can lead to the discovery of knowledge that might be disastrously misused. He believes that such a principle, if consistently applied, would paralyse all research: "It is hard to think of an area of scientific research that *could* not lead to the discovery of potentially dangerous knowledge." While Stich gives serious attention to the use of probability estimates of biohazards, he neglects to apply similar reasoning to the application of research programmes. The potential for misuse of science is not distributed uniformly among all research enterprises; consequently, some may warrant greater social control than others.

Carl Cohen, in his essay "On the Dangers of Inquiry and the Burden of Proof", wields a philosophical scalpel to the critics of recombinant DNA research. He skillfully dissects their arguments, exposing lack of rigour and their weak analogical reasoning and use of criticism, to which no response is possible ("heavy question arguments"). Cohen's reconnaissance of the terrain of criticism is limited to the most radical critics. Moreover he says nothing about the faulty reasoning and emotional responses of proponents of laissez-faire science. There, too, one finds arguments built on conjectures and quasi-scientific findings.

This is the first collection of papers on the recombinant DNA debate by a major publisher for a non-technical audience that addresses scientific, philosophical and policy issues. The essays are generally of high quality. They centre around the controversy in the US up to 1977. Since that time new issues have surfaced including the patenting of novel life forms, the rise of commercial interest in recombinant DNA techniques, the health of workers in large scale fermentation plants, and the disposal of by-products in production.

The weakness of this collection is in its failure to cover the political and sociological context of the debate. With the slight exception of an essay by sociologist Max Heirich on how the funding of science affects decision-making about science, there is no treatment of the key determinants that shaped DNA policy in the US. Factors of interest are: the

effectiveness of the scientific lobby; the commercial ties of scientists in the recombinant DNA field; the control of the risk assessment process; the ability of scientists to contain the issues to laboratory biohazards; the role of environmental groups; and the politics of the Recombinant DNA Advisory Committee.

We shall await another collection of papers to bring the issues up to date and address these critical factors. □

Sheldon Krinsky is Acting Director of the Program in Urban Social and Environmental Policy at Tufts University, Medford, Massachusetts.

Synthetic biology

Richard Roblin

A Double Image of the Double Helix: The Recombinant DNA Debate. By Clifford Grobstein. Pp. 177. (Freeman: San Francisco and Reading, UK, 1979.) Hardback £6.90; \$11; paperback £3.50; \$5.95.

THE tone of books about the recombinant DNA policy debate has both reflected and fueled the intensity of public concern. As the debate grew heated during 1976–78, books by journalists and science-writers vividly detailed the early history of the controversy, and discussed possible biohazards. In the quieter atmosphere of 1979, Clifford Grobstein has contributed a balanced, analytical view of the American sector of the recombinant DNA landscape which emphasises the science and public policy issues thrown up by the turmoil. In doing so, he has written an excellent primer for the next stage of discussion about recombinant DNA policy issues.

Grobstein's book will be read with profit by a variety of readers. Here, interested members of the public will find an outline of the relevant science, a history of the controversy, and thought-provoking discussions of exploration, risk and research regulation. Scientists should find interesting Grobstein's interpretations of the social and political context of their research, even though they may not like the world which he describes. Bureaucrats and legislators should ponder Grobstein's comments on the incompleteness and instability of current public policy on recombinant DNA research. In Grobstein's opinion, failure to extend application of the NIH Recombinant DNA Research Guidelines to industrial as well as academic research risks undercutting their effectiveness.

One of the major sections of the book deals with the issues surrounding regulation of basic research. Grobstein finds such regulation generally distasteful, and articulates several requirements for sound regulation of research. He views continued research and expansion of human knowledge as "essential to the public interest", and would restrict these

only when "there is compelling evidence of clear and present danger." However reassuringly familiar this criterion sounds to American ears, how would it apply in the recombinant DNA case? The conjectural nature of recombinant DNA biohazards remains the central intellectual dilemma of recombinant DNA policy. Except for intentionally malevolent applications, there never was, and may never be, compelling evidence of clear and present danger in the use of recombinant DNA techniques. What policy to follow given this uncertainty remains the central issue of the recombinant DNA debate. Does this mean that Grobstein believes the guidelines approach and the concomitant public and legislative furore to be an example of unsound regulation? He doesn't say, and I believe he would have made his book better if he had been more specific in this and several other places.

One thorny problem associated with the recombinant DNA debate is the role of the public in policy formation. If there are conjectured risks to public well-being because of the use of recombinant DNA techniques, then should the public have a say in how these techniques are to be used? Grobstein points out the tendency to apply criteria and procedures developed for regulation of human experimentation to recombinant DNA research. This analogy led some to suggest that appropriate policy for recombinant DNA research required something like a public 'informed consent' before proceeding with widespread use of the technique. Grobstein raises, but does not directly answer, the question of whether this extension of the principles of risk-benefit calculation and informed consent is appropriate for research in general (or recombinant DNA in particular). My own feelings are that these criteria are not appropriate where risks are conjectural, because meaningful risk-benefit estimations cannot be made. In addition, why single out the area of recombinant DNA research, when public "informed consent" has not been seriously urged in other research situations (for example, deepspace exploration) where risks could also be conjectured?

Inevitably, in an area as fast moving as recombinant DNA research, the pace of new discoveries outstrips the rate at which books can be conceived, written and published about them. Thus, Grobstein mentions only in a footnote the recently discovery that the DNA sequences which

code for several eukaryotic viral and cellular proteins are not all adjacent to one another as they are in bacterial DNA. The discovery of 'split genes' and RNA splicing in higher eukaryotic cells, and the lack of evidence for RNA splicing mechanisms of comparable specificity in *E. coli*, have led many scientists to conclude that split eukaryotic viral and cellular genes will not be correctly translated into functional proteins in *E. coli*. If many eukaryotic genes are split and cannot produce functional proteins in *E. coli*, then the chance of producing pathogenic *E. coli* through 'shotgun' cloning of eukaryotic DNA segments is reduced still further. These arguments were partly responsible for the considerable reduction in containment for such cloning experiments in the December 1978 revision of the NIH Guidelines. It is unfortunate that Grobstein was unable to include the impact of this new information in his discussion of potential risks in recombinant DNA research.

Grobstein ends his book with a suggestion that a presidential study commission be appointed to work toward a comprehensive assessment of issues generated by the recombinant DNA debate. He feels that this would create a needed arena "in which all issues can be examined and which gives full access to all interested parties and experts". However, since Grobstein's book was written, there have been significant changes in both the content and administration of American recombinant DNA policy. Estimates of the possible risks of recombinant DNA experimentation have dropped further. Accordingly, containment requirements for several types of experiments have been reduced, and significant supervisory authority over recombinant DNA experiments has been delegated to local Institutional Biosafety Committees. The NIH Recombinant DNA Advisory Committee (RAC) has been enlarged to 25 members, thus expanding its expertise and diversifying it politically. Meetings of the RAC have become a national forum for debating and voting to recommend changes in the NIH Guidelines, the chief ingredient in current American recombinant DNA research policy. RAC procedures, which provide for prior publication of proposals to be discussed and publicly accessible meetings, have opened a permanent channel for public input into decision-making on recombinant DNA research policy. In addition, the major scientific and procedural objections of critics like Sinsheimer, Wald and King have either been accommodated or been found to be generally unpersuasive. In the light of these recent developments, one wonders whether Grobstein would continue to advocate a presidential study commission.

Given the current trend, we are at the beginning of a period in which the NIH Guidelines will be partially or completely

dismantled. Some scientists believe that it will be possible to stuff the genie of regulation of recombinant DNA research back into the bottle. If so, what kind of a legacy will the recombinant DNA debate leave? Perhaps it is too early to clearly assess this question, but the following thoughts come to mind. The development and evolution of guidelines for recombinant DNA research provides a case-study in innovative formation of a policy to cope with uncertainties generated by a major expansion in human knowledge and power. Early discussion of the possibilities in public, a continuation of cautious research coupled with risk-assessment studies, and built-in mechanisms for modifying regulations in the light of new

knowledge may prove to be useful principles in analogous future situations. In addition, the recombinant DNA debate has conveyed to a wide audience the vast potential of the 'synthetic biology' opened up by recombinant DNA techniques. Thoughtful consideration of the ends to which this potential is being and could be applied should commence, as concern over potential biohazards diminishes. □

Richard Roblin was a member of the National Academy of Sciences Committee on Recombinant DNA Molecules and the organising committee for the 1975 Asilomar Conference on Recombinant DNA Molecules. He is now Head of the Molecular Biology of Tumor Cells Group, Cancer Biology Program, Frederick Cancer Research Center, Frederick, Maryland.

Drives and action patterns

John R. Krebs

The Origins and Rise of Ethology: The Science of the Natural Behaviour of Animals. By W. H. Thorpe. Pp. 174. (Heinemann Educational: London, UK; Praeger/Holt, Rhinehart and Winston/CBS: New York, 1979.) £5.90.

THIS book is an extended version of the first Niko Tinbergen lecture, given by Professor Thorpe to the Association for the Study of Animal Behaviour in 1974. He describes how ethology started, what it was like in the middle of the twentieth century and what it is about today. The middle section of the book, which is full of anecdotes and personal recollections of Professor Thorpe, is to my mind the best.

The early history of ethology is traced by Thorpe to John Ray, the seventeenth century British naturalist who, among many other things, did experiments on clutch size in birds. The subject in its present day sense (the naturalistic study of animal behaviour; not the "science of character-formation" as in the term used by J.S. Mill) emerged in France in the eighteenth and early nineteenth centuries through the writings of C.G. Leroy, J.B. Lamarck and E. Geoffroy-Saint-Hilaire. (Some readers may be amused to know that Leroy was gamekeeper of the area in France called Marly — virtually the same name as that given to the wood near Oxford in which R.A. Hinde carried out his thesis research nearly 200 years later.) Although Britain had a strong tradition of country naturalists in the eighteenth and nineteenth centuries, Thorpe rightly emphasises D. Spalding as the key British figure in the early development of ethology. Spalding pioneered experimental studies of behaviour development and had a great

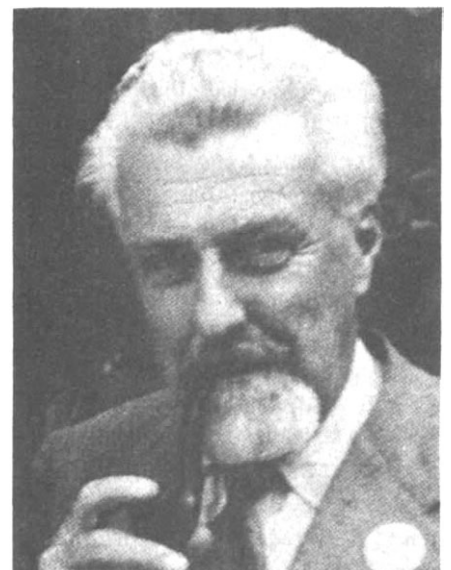
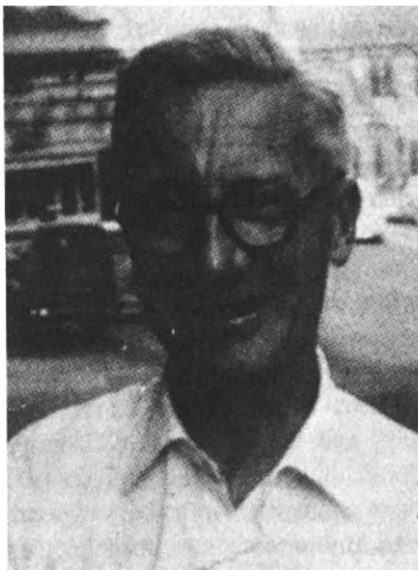
impact on Lloyd Morgan, who was influential in espousing a scientific, reductionist approach to the study of animal behaviour. Among early American students of behaviour, Thorpe mentions particularly the contributions of Whitman, Craig, Lashley and Wheeler; perhaps he should also have included W.C. Allee whose book *The Social Life of Animals* foreshadowed much that is current in ethological thinking.

From this straightforward historical account, Thorpe moves to the period with which he is familiar from personal experience. In the 1930s and 1940s ethology became firmly established as a discipline distinct from other approaches to the study of behaviour, mainly through the work of Lorenz and Tinbergen. The account of this period is very revealing to those who have seen only the later years of the era of these great men. Today, Lorenz's theories are viewed as somewhat old-fashioned and naive, but as Thorpe stresses "The very fact that Lorenz's early papers now appear so outdated is a tribute to their effectiveness . . . It is the impetus which they gave to experimental work which has,

in a sense, rendered them so quickly out of date, although they are still of course extremely well worth reading".

According to Thorpe, the central problem facing ethologists in the 1930s was to elucidate the nature of instinctive behaviour. Although it was widely recognised that animals perform complicated "goal oriented" sequences of behaviour, such as nest-building and courting, without any particular training, there was no conceptual framework within which to analyse and dissect these instinctive behaviours. Lorenz provided the framework in a series of papers published in the decade 1931-41. Instincts were viewed as being made up of simple stereotyped, inborn movements (fixed action patterns) linked together by more flexible and modifiable goal oriented behaviour (appetitive behaviour). Both of these were thought to be driven by "specific drives" (physiological mechanisms). Usually the fixed action patterns were released by a specific stimulus (releaser) and they were consummatory in the sense of dissipating the specific drive for that appetitive behaviour and fixed action pattern sequence. Internal drive was considered to then gradually build up until a fixed action pattern could discharge it again. If no suitable stimulus appeared, the action might go off "in a vacuum". Professor Thorpe stresses that this theoretical framework was valuable because it immediately led people to investigate in detail the nature of instinctive behaviour. For example, physiological and endocrinological studies of drives, perceptual studies of releasers, and genetic studies of fixed action patterns were set up to test Lorenz's ideas.

While providing a lucid account of Lorenzian theory, Professor Thorpe also tells us many anecdotes from the immediate post-War years. Stories are told of how Lorenz nearly went to Cambridge



Niko Tinbergen and Konrad Lorenz in Cambridge, 1959

instead of to the Max Planck Institute; how Lorenz and Tinbergen quacked like ducks to put off two predatory women; and how Thorpe himself was asked to present a paper of "about two hours" when he turned up at the First International Ethological Conference! It would be nice if this part of the book were expanded into a full volume at a later date.

The last chapter, on the present position of ethological concepts and research, is also fascinating from an historical viewpoint. It illustrates how the same events can be seen in a totally different light by observers from two different generations. In Thorpe's view, ethology today still works within the Lorenzian framework, and the questions asked still deal with fixed action patterns, drive, displacement activities, releasers, and so on. The details have changed very much, but the conceptual armoury is still the same. To an ethologist trained a generation later, the view is that ethology (in particular British and American ethology) underwent

a purge in the 1950s and early 1960s, mainly due to the masterly critiques of R.A. Hinde; in this much of the earlier Lorenzian theorising was rejected and replaced with a hard-headed, reductionist approach. This created a spartan atmosphere in which theorising was definitely out, and hard data in. Then the early 1970s saw a flowering of new theoretical ideas and new questions about behaviour, this time linking ethology with population genetics and evolution. Perhaps there will be a new purge in the 1980s.

Neither of these contrasting views about present-day ethology can be said to be right or wrong: they emphasise that in spite of our attempts to be objective about the behaviour of animals, the interpretation of our own history is very much subjective. □

John R. Krebs is Lecturer in Zoology at the Edward Grey Institute of Field Ornithology, University of Oxford, UK.

Selected genetics

M. J. Lawrence

Understanding Genetics. By E.B. Ford. Pp. 201. (Faber and Faber: London, 1979.) £7.25.

PROFESSOR FORD tells us in the preface that this book is an attempt to meet the needs of those who, whether they be men of general education or scholars in other fields of learning, wish to know something of the theoretical aspects of genetics. This is a laudable, though ambitious, objective, for if such an attempt is to succeed, the author will have to possess an unusually wide and deep knowledge of the subject, so as to be able to give both an adequate coverage of it and to deal with open questions in a fair and unbiased way. To what extent does Professor Ford's new book meet this requirement?

The book contains eight chapters which deal with the Principles of Genetics; Sex; Evolution; Polymorphism and Mimicry; Industrial Pollution; Genetics in the Countryside and Garden; Individual Variation in Man; and Genetics and Human Societies. The contents of the book reveal that Professor Ford's coverage of the subject is far from complete, for he deals only with some aspects of classical, human and what he has called ecological genetics. There is nothing about molecular or microbial genetics, despite the fact that these are now the most actively researched areas of the science and are, moreover, ones which raise problems of great interest to the layman. This omission,

furthermore, is no mere oversight, because we are told that the structure of DNA is "much beyond what is appropriate for a book of this kind" (page 30). This is surely a serious error of judgement. The reader will look in vain, therefore, for enlightenment on why, for example, there has been much public debate on the subject of genetic engineering. For this they would have to look elsewhere.

Those who are familiar with Professor Ford's style will know what to expect from this book; nor will they be disappointed, for here again we find his characteristic, enthusiastic and authoritative treatment of the subjects with which he deals and also a number of amusing and illuminating anecdotes, including one about how to plan for a scientific camp. Indeed, the book seems to be derived from two of Professor Ford's previous books, *Ecological Genetics* and *Genetics for Medical Students*, and is therefore something of an intellectual biography of his work. Those who are familiar with this work, however, will also know that there is by no means general agreement on some of the matters that are discussed. For example, apart from the obvious exception of sickle-cell anaemia, there is almost no evidence to justify the confident statement on page 151 that "heterozygous advantage is the usual method for maintaining polymorphic variation", though it is, of course, possible that some polymorphisms are maintained in this way. Then again, we do not know "that it is usual for" selective advantages "to reach 20 or 30 per cent, often much more" (page 69). The layman, however, will be unaware of these biases and hence is likely to be seriously misled when he goes on, as Professor Ford hopes he will, to pursue his interest in genetics in

other works.

There are, unfortunately, other errors of emphasis and, indeed, of fact in the book. For example, we are told on page 155 that "it would be highly *suspicious* [my italics] if a pair of blue- or grey-eyed parents had a child with dark-brown eyes". While such an outcome would be unusual, such cases have occurred in circumstances where the paternity of the child was beyond reasonable doubt. Then again, I know of no evidence to justify the statement on page 74, concerning the pairing of homologous chromosomes during the first division of meiosis that "allelic attraction must be stronger when the pairs are identical (homozygous) than when they are dissimilar (heterozygous)". Is it really the case that Man is more variable than other species (page 13) and that among our races, the Japanese are "much the less diversified" (page 172)? There is a particularly misleading error in the simple numerical example on page 28 which Professor Ford uses to explain how the order of genes along a chromosome may be determined from the results of a three-point backcross (his ACB should be BAC). On page 57 we are told that if "we keep organisms in a strictly constant condition in the laboratory, all their variation is [my italics] genetic" (would that this were true!). The simple method for the detection of heterozygous advantage given on page 107 is unsatisfactory because the X^2 in question can be significant in the absence of this type of selection. Lastly, on page 116, where Professor Ford writes, about self-incompatibility in those species in which this is determined by a single, multi-allelic gene and control of the pollen reaction is gametophytic, that: "If both the male and female plants possess, for instance, S2 and S2 (one carried by the pollen, the other possessed by the stigma) fertilisation fails". This statement is highly misleading because it is true if and only if the comment in parenthesis is ignored (if the latter were correct the cross would be compatible). There are a number of other errors in the book, including some concerning page and author references; and the way in which some of the subject material is dealt with in the last two chapters of the book made this reader uneasy.

Reviewing this book has been a painful task, because I, like many of my colleagues in the field of ecological and population genetics, owe Professor Ford a great debt; he is one of the pioneers of the subject and has made many distinguished contributions to it. But in view of the stated aims of the book, we have a wider duty to those people for whom it is intended. With this in mind, the book cannot be recommended to the layman. □

M. J. Lawrence is a Senior Lecturer in the Department of Genetics at the University of Birmingham, UK.

Illuminating astronomy

Owen Gingerich

Man's View of the Universe: A Pictorial History. By G.E. Tauber. Pp. 352. (Crown: New York, 1979.) \$19.95.

TAUBER'S elucidation of "evolving concepts of the universe from ancient times to today's space probes" belongs to the genre of history of astronomy in the service of popularisation. He thus joins the class whose predecessors range from Camille Flammarion to Patrick Moore and Fred Hoyle.

An historical approach is particularly felicitous for astronomy, with its long and nearly continuous development. It has the advantage of starting with the simplest observations and theories, which can introduce the novice to the sky as it still appears. The story then leads through the drama and pathos of Galileo, to the puzzling and curious genius of Newton, and finally in a modern climax to Einstein and relativity. Tauber exploits the anecdotal and the picturesque to leaven what is essentially a popular textbook, and in so doing produces a guide to modern astronomy far more readable than the typical elementary textbook. He is obviously most at home with relativity and with cosmology, and there his presentation is outstanding. But the subtitle, *A Pictorial History*, promises us more than a mere textbook, and alas from either the pictorial or historical viewpoint the book is a

considerable disappointment.

There are, to be sure, hundreds of illustrations, which in effect form a separate and parallel account, unreferenced and almost completely unlinked with the running text. Some of them are fresh and attractive, such as the pair of portraits of Wilhelm IV of Hesse and his wife, the Foucault pendulum in the Pantheon, or Robert Goddard beside an early liquid rocket. However, many are commonplace and often poorly reproduced; a significant proportion of the illustrations are line diagrams, which emphasise the textbook aspects to the detriment of the historical qualities.

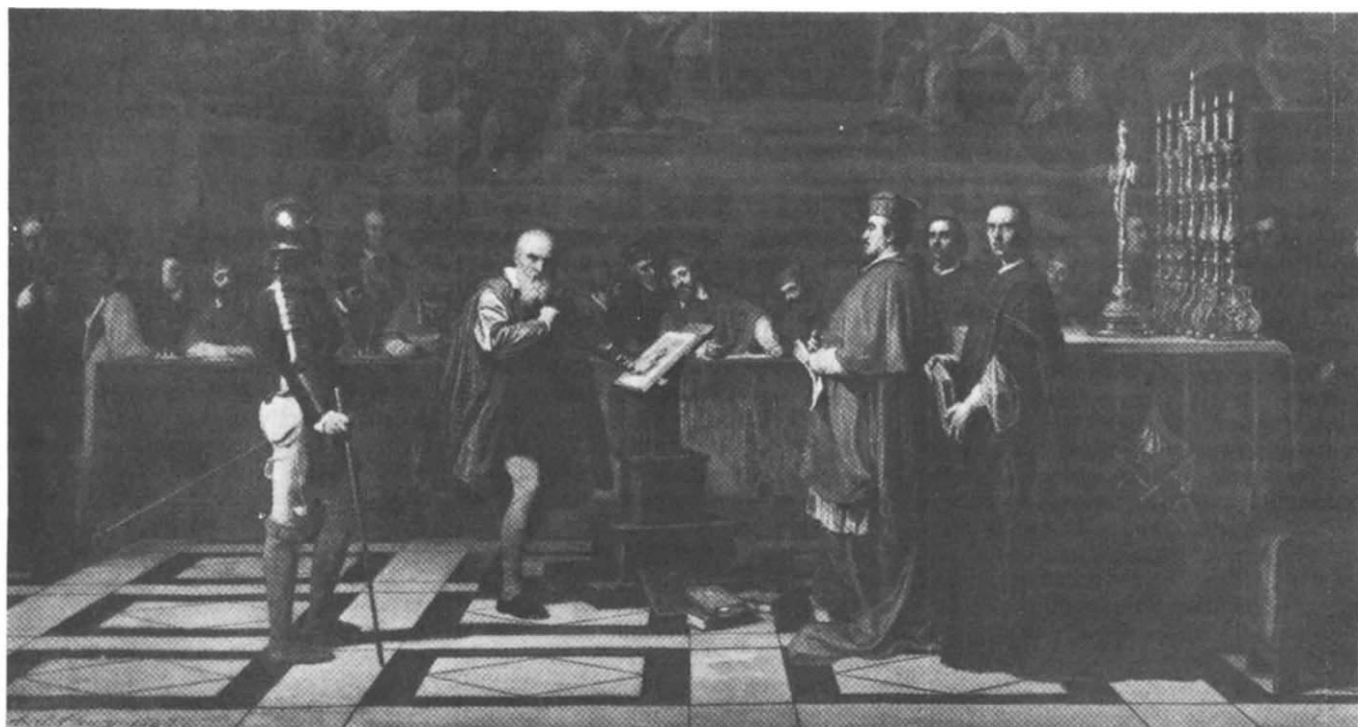
Consider, for instance, the section on Newton: the best of the illustrations is a fine manuscript drawing of Newton's telescope, and there are halftones of Newton, Woolsthorpe, a modern painting of Newton with his prism, plus muddy views of Huygens and conic sections. But these are overwhelmed by a score of diagrams representing everything from the graph of an inverse square law, a hopelessly wrong scheme of recombining coloured light with a second prism, a redrawing of Newton's famous (and incorrect) diagram on free fall from his letter to Hooke, precession, tides, and so on. The Newtonian section epitomises the pictorial problems of the entire work: squeezed and uninviting layouts, erratic quality of reproduction, and uninspired typography. It would be heartless to dwell further on these inadequacies, for which the publisher is probably more to blame than the author.

Several pictures are erroneously captioned or credited. The widely copied traveller poking his head through the vault of the heavens to see the celestial gearwork beyond is here reproduced as a sixteenth-

century woodcut, although it is now definitely established as late nineteenth-century art nouveau, probably from the hand of Camille Flammarion. It is hard to believe that the photograph purporting to be the Magellanic Clouds on page 241 really shows those objects. On page 36 there is "an artist's view (date unknown) of Thales' universe", in the public domain according to the list of credits. In fact, the figure was specifically drawn for Carl Sagan's Time-Life book, *Planets* (1966). The drawing that decorates the title page has been adapted from the same source.

As a pictorial *history*, Tauber's production fares even worse. Factual errors abound. Contrary to his text, there is absolutely no evidence that Copernicus had to occupy himself with astrology (page 98), and in Kepler's music of the planets, the faster the planet, the higher the notes (page 124). Galileo's telescope did not contain three convex lenses (page 196), and Herschel never became Astronomer Royal (page 212).

Actually such flaws are rather minor, and although they detract from the book's reliability, they scarcely interfere with its pedagogical exposition. What dismays the historian of astronomy far more than a peppering of factual errors is the writing of "Whig history". That expression, introduced by Herbert Butterfield, refers to history seen from the vantage point of the victor; in the history of science, it means evaluating the past in the light of today's theory. It is Whig history of science, for example, to give the ancient heliocentric schemes of Aristarchus any special prominence. As physicist-historian Stephen Brush has said, credit for discovery should be given not so much for the originality of the concept as for the persuasiveness of the arguments; certainly



the single sentence that has come down from antiquity about Aristarchus' cosmology contains no persuasive arguments.

Tauber gives a column to Aristarchus but his Whiggishness is generally more subtle, precisely the kind that distinguishes textbooks and popular science from history. In describing the distances of stars, he goes straight to the trigonometrical parallaxes finally established by 1840, thus ignoring the intellectual breakthrough of the late seventeenth-century when astronomers recognised that stars were really distant suns and when they began to calculate reasonable distances photometrically. Similarly, in telling of Huygens' discovery of the rings of Saturn, he places this in the context of building better telescopes, not realising that the Dutch astronomer made his interpretation in mind's eyes at a time when the ring system was actually edge-on and invisible.

Tauber's presentation is rich in chronological facts rather than the historical facts that illuminate the actual process of discovery. In introducing galaxies under the heading 'Island Universes' he alludes to Kant, Messier, the Herschels and Lord Rosse in a swift succession leading to the Shapley-Curtis debate in 1920.

He refers implicitly to the rotations of spiral nebulae found by van Maanan, but by Whiggishly suppressing explicit mention of these now-discredited measurements, he plants a confusing discontinuity into his story. Nor does he mention novae or red shifts, because he sorts these key elements in the historical account into other bins. There is nothing reprehensible about organising the material this way for instructional reasons — indeed, it probably leads more rapidly to an understanding of our modern ideas of the Universe.

In contrast, it is the task of the historian of science to show the development of science as a creative human activity, which for past science requires a sympathetic reconstruction of the motivations and limitations of a bygone period; this demands a selection of those facts that illuminate the understanding at that time, not the rather different group of facts now woven into our contemporary knowledge. I suspect that most prospective owners of Tauber's *Pictorial History* will be quite satisfied to get a relatively painless and accurate survey of modern astronomy, and would probably be disappointed if they got serious and accurate history of science. My plea to my scientific colleagues is that Tauber's work should be seen as a somewhat successful popularisation of science, but not as history of science. □

Owen Gingerich is Professor of Astronomy and of the History of Science at the Harvard-Smithsonian Center for Astrophysics, Cambridge, Massachusetts.

Prehistoric Avebury

R.J.C. Atkinson

Prehistoric Avebury. By Aubrey Burl. Pp. 275. (Yale University Press: New Haven, Connecticut, and London, 1979.) \$19.95; £8.95.

NEXT to Stonehenge, Avebury is better known than any other prehistoric monument in Britain. About Stonehenge countless books have been written, good, indifferent and frankly lunatic; but about Avebury very little, even though, in the words of its first recorder, John Aubrey, it "does as much exceed in bigness the so renowned Stonehenge, as a Cathedral doeth a parish church". It has not escaped, even recently, the weird and uncritical lucubrations of the lunatic fringe; but until now there has been no comprehensive treatment of Avebury and its archaeological setting which could rival William Stukeley's *Abury* of 1743. This is not to ignore, of course, Dr Isobel Smith's *Windmill Hill and Avebury* (Oxford University Press, 1965) or *The Avebury Monuments* (HMSO, 1976) by the late Faith Vatcher and her husband, which are primary sources; but the first is an excavation report, and the second a concise guide for the visitor.

Aubrey Burl has now turned from British stone circles in general, on which he is the main authority, to a detailed study of one of the best known of them, on a scale and with a breadth of knowledge and vision rivalled only by Stukeley. This is a quite remarkable book, and a pleasure to read. It is intended for the intelligent layman, and in its presentation it has many of the attributes of more expensive 'coffee-table' books, with large format, well-spaced type and lavish illustrations, including more than a dozen full-page colour plates; but it also contains a very full set of notes and references, a comprehensive bibliography and a well-designed index.

The specialist reader (and maybe others as well) must make full use of the index, because the treatment is markedly discursive and the discussion of parts of Avebury, and of neighbouring sites, is widely dispersed throughout nine chapters. These are thematically arranged, with an underlying but not explicit chronological order, which is not that of the chronology of Avebury itself. As one familiar with the monuments from childhood, and with something of their archaeology from adolescence, I find this confusing and sometimes irritating; but I am not perhaps the reader Burl had in mind.

Throughout the book Burl has used his very wide reading to draw parallels between

the available archaeological evidence, from Avebury and neighbouring sites, and sometimes from more distant sites in Britain, and ethnographical observations from other parts of the world, principally the documented customs for the living and the dead amongst various tribes of North and Central American Indians.

Some of these likenesses are so striking that the lay reader may be tempted to fall inadvertently into a logical trap, and to suppose that "because it could have been like that, therefore it was". Burl is obviously aware of this danger, and has taken some care, though perhaps not quite enough, to warn his readers of the pit-falls of facile conclusions based on comparisons of very different contexts in time and space, and of very diverse economies and environments. In the end ethnographic parallels can serve only to enlarge the field of conjecture of the prehistorian. They cannot tell us what our own past was, because this is unknowable in all but a trivial sense.

In the penultimate chapter ("The Purpose of Avebury") the author boldly gives his view, with suitable cautions, about the funerary and fertility rituals for which Avebury may have been built. Here, and indeed throughout the book, he displays the vision of a creative artist, in putting flesh and colour upon the bare bones of the archaeological evidence, no less pitifully exiguous here than in the other stone circles that he has studied. Amongst contemporary writers on prehistory he has the rare and enviable gift of evoking for the mind's eye the past-which-might-have-

Sorry, for copyright reasons some images on this page may not be available online

been, without ever departing so far from the raw evidence as to strain the credence of the reader.

This admirable but discursive recension raises many questions about what is still unknown. Some of these can and should be answered, and soon, as far as available techniques allow.

In particular, the chronology of Avebury is still guess-work. On page 166 Burl gives a table of dates which divides the building of Avebury into three phases (interior stone circles; earthwork and main circle; avenues). This is plausible on the evidence available; but it is based wholly on the dating by analogy of pottery types, which is notoriously uncertain. The surviving finds from excavations can surely yield a suitable series for radiocarbon dating. Could not this be undertaken by the Department of the Environment, the official guardians of the monument?

Likewise, the former positions of the missing stones in the North and South circles, and in the eastern half of the great circle inside the ditch, still await identification. So do the stone-holes and buried stones of the Kennet Avenue, beyond the part excavated by Keiller and Piggott, and almost the whole of Stukeley's Beckhampton Avenue to the south-west. The latter, long regarded as the illusory product of Stukeley's perfervid imagination, has now been restored to credibility by recent finds. Further confirmation is needed, if the full extent of the Avebury complex is to be understood.

To search by excavation would be premature, because all excavation destroys more evidence, unrecognised, than it yields to the most skilled, experienced and conscientious excavator. The state of the art has not advanced so far beyond the work of the 1930s as to justify further knowing destruction.

There are, however, techniques of geophysical survey which can be applied, some of them developed specifically by the Ancient Monuments Laboratory of the Department of the Environment. There is a case here for a long-term programme of research, in which the diagnostic use of the simple hand-held probe should not be neglected. It is one of the defects of this book that these future problems are not spelled out, with non-destructive solutions (or at least programmes) of this kind.

There are other defects too. The values used by the author (page 175) in calculating the man-hours required for the building of the Avebury earthwork are grossly in error; but the corrections are largely self-cancelling, so that the result is still about 1.5 million man-hours. His second estimate (pages 175-76), which is about half of the first, is invalid because it is based on the raw evidence from the experimental earthwork on Overton Down, and makes no allowance for the scale-factor required. This is included in my own empirical formula on which the first estimate is founded.

Furthermore, although the neighbouring Neolithic causewayed camp on Windmill Hill, and the West Kennet Long Barrow, are discussed and interpreted in detail in the text, no plan is given of either. Worse still, there is no modern plan of Avebury itself, with the stones numbered, although individual

stones are often referred to by their numbers in the text. These omissions mar what would otherwise be a quite excellent book. □

R.J.C. Atkinson is Professor of Archeology at University College, Cardiff, UK.

Boswellian enthusiasm for science

M. Rowan-Robinson

Broca's Brain: Reflections on the Romance of Science. By Carl Sagan. Pp.347. (Random House: New York; Hodder and Stoughton: London, UK, 1979.) \$12.95; £6.95.

By his clear and witty writing and by his willingness to write about those eternally popular subjects, the planets and life on other worlds, Carl Sagan has captured a large audience. His last book *The Dragons of Eden*, on the evolution of human intelligence, won him a Pulitzer Prize, and the present book is already high on the American bestseller list. Sagan is a real phenomenon and we have to take him seriously as a major populariser of science today.

Broca's Brain opens with a superb evocation of the inner recesses of the Musée de l'Homme in Paris, where Sagan finds and muses on the preserved brain of Paul Broca, a pioneer of neurosurgery and anthropology in the mid-nineteenth century. This could almost be the opening of a novel in the manner of Balzac. The themes of the book are "the joys and social consequences of the scientific endeavor; borderline and pop science; the not entirely different subject of religious doctrine; the exploration of the planets and the search for extraterrestrial life; and Albert Einstein . . .". The disparate nature of these themes is matched by an almost complete absence of continuity between the chapters of the book. This is a collection of lectures which Sagan has given on various occasions and of articles that have appeared in magazines as diverse as *Scientific American* on the one hand and *Playboy* and *TV Guide* on the other.

Although it is disappointing that these themes are not developed in the coherent and sustained way that we would expect from a purpose-written book, these essays are lively and entertaining, bubbling with amusing anecdotes about science and scientists. Sagan would make an excellent scientific Boswell. I particularly liked "A planet named George", about how the planets, satellites, and their craters and mountains, have come to have their exotic

names. Not many people will be aware that the satellites of Jupiter are named after the illicit loves of his Greek counterpart, Zeus. Sagan feels it is rather unfair that Zeus' wife Hera does not get a mention. There is a marvellous, absurd picture of the international astronomical committee which decides these matters worrying about whether the Third World is sufficiently represented in the names of craters and asteroids and deciding that maybe some other creative humans besides astronomers and astronomers' wives ought to be so honoured.

However, Sagan aspires more to the role of Johnson, the moralist. He has a rather uncritical enthusiasm for science and technology and deplores the "sparse, unimaginative and ineffective efforts at science education" of American media and schools. He sees the best protection against abuses of science as a scientifically literate populace. "In exchange for freedom of inquiry, scientists are obliged to explain their work". But Sagan, while apparently admiring the anti-militaristic activities of Einstein and Russell, does not face up to the issue of military research, that all the most dangerous research (nuclear weapons, germ warfare and so on) is controlled by governments in an atmosphere of rigid secrecy.

There are a series of essays on pseudoscience and fringe science: astral projection, spirit rapping, precognitive dreams, UFOs, Velikovskianism, and so on. There is a particularly good essay on the problem of the remarkable astronomical knowledge of the Dogon

Sorry, for copyright reasons some images on this page may not be available online

people of Mali. As Sagan points out, their astronomical knowledge is just not remarkable enough to have been learnt from little green men in UFOs and could all have been learnt from contacts with Europeans. Sagan has performed a useful service here in collecting together these examples of public gullibility and demonstrating how a mixture of deliberate fraud and uncritical thinking has allowed millions to be bamboozled throughout history.

Yet when later in the book Sagan turns to discuss religion, his own critical apparatus seems to be switched off. "These mystical insights must mean something . . . If religions are fundamentally silly, why is it that so many people believe in them?" — an argument which could equally be applied to belief in UFOs or astral projection. Sagan's excitement by the phenomenon of mystical visions, and his curious attempt in the last chapter of the book to link these and all religious ideas to experiences associated with birth, suggest that Sagan is about to become a "born-again" believer in — something.

Although Sagan is rightly caustic about some of the absurdities of the popular pseudosciences he makes no effort to discuss the problem of demarcation between science and pseudoscience, which has so occupied the attention of Karl Popper and his followers. Sagan's championing of science seems positively naive at times. Compared with the doctrines of pseudoscience " . . . science is more intricate and subtle, reveals a much richer universe and powerfully evokes our sense of wonder. And it has the additional and important virtue — to whatever extent the word has any meaning — of being true". Astrologers would obviously be happy with this statement with the word "astrology" substituted for "science". That is not what distinguishes science from pseudoscience.

On the exploration of the Solar System, Sagan is naturally interesting and thorough, for this is his own area of expertise. It would be interesting some day to hear what it is like for a scientist to work on one of these NASA missions. I find it rather touching that Sagan's belief in the existence of life elsewhere in the Universe is so passionate that he cannot bring himself to mention NASA's official interpretation of the Viking Lander mission to Mars, namely that Mars is chemically but not biologically active.

In comparing Sagan with popularisers of astronomy like Hoyle or those grand old rivals Eddington and Jeans, it has to be said that he has so far set himself an easier task. Those earlier masters set out to popularise the astronomical research of their times: they were ahead of the tastes of their public and tried to take their readers with them into the world of the modern astronomer. Carl Sagan, like the effervescent Patrick Moore, talks for the most part about the areas already popular with the public: the

Solar System, space travel, life in the Universe. Sagan's references to the "new" astronomies, radio, infrared, X-ray, and so on, seem to me to be perfunctory. He is not even particularly good on a topic which might be expected to have appealed to him, astronomy from space platforms. He refers to "an astronomical telescope in earth orbit called Copernicus", without mentioning that it is primarily the ultraviolet band that the instruments on the Copernicus satellite have opened up. He seems to think that X-ray emission from gas in clusters of galaxies was discovered by the recent HEAO satellites, whereas this was one of the achievements of the pioneering Uhuru satellite launched in 1970.

Considering that most of this material has been seen or heard by the public before,

there are a couple of minor errors that ought to have been removed by now. It is not the orientation in space of a molecule that is quantised (page 17) but its angular momentum or energy. And galaxies do not disappear from view over the event horizon (page 296): on the contrary they swim into view over it. And as for the suggestion that psychedelic molecules exist in great abundance in plants because of artificial selection as a result of cultivation by human beings. . .

But these reservations do not diminish my enjoyment of the book. *Broca's Brain* is an entertaining collection of essays by a very good popular-science writer. □

Michael Rowan-Robinson is Reader in Astronomy at Queen Mary College, University of London, UK.

In the conflux of eternities

Freeman J. Dyson

In the Centre of Immensities. By Bernard Lovell. Pp. 174. (Hutchinson: London; Harper and Row: New York, 1979.) £5.50.

LOVELL'S life-work has been the exploration of the Universe by means of radio-telescopes. He was one of the small group of pioneers who understood thirty years ago that the new science of radio-astronomy would give us a wider and deeper view of the Universe than optical observations alone could provide. The achievements of the telescopes which he built have proved his vision right. In our modern theories of the structure and development of the Universe, the evidence obtained from radio observations plays a central and indispensable role.

In this book Lovell is not concerned with his own work as an observer. He is describing the historical growth of our understanding of the size and shape of the Universe and of our own situation within it. He puts this astronomical history within the context of the wider philosophical and religious struggles which have raged around the growth of modern science. He believes, in opposition to the prevailing fashion of scientific positivism, that the creative interaction between astronomy, philosophy and religion is not yet at an end. His purpose is to demonstrate that the discoveries of the past fifty years have confirmed rather than contradicted the words spoken by the mathematician-philosopher Whitehead in 1925: "When we consider what religion is for mankind, and what science is, it is no exaggeration to say

that the future course of history depends upon the decision of this generation as to the relations between them."

To readers moderately conversant with the facts of astronomy, Lovell's expository chapters describing the growth of astronomical knowledge will be easy to follow but not particularly novel. On the technical level, his exposition does not differ substantially from the accounts given in other popular books such as Steven Weinberg's *The First Three Minutes* (André Deutsch/Fontana: London; Basic Books: New York; for review, see *Nature*, 267, 291; 1977). The exciting things in Lovell's book are non-technical. His unique quality as a thinker is displayed in the philosophical and ethical discussions with which the book begins and ends, and in the breadth of his knowledge of history and literature. Chapter 1 starts with Saint Thomas Aquinas and ends with Thomas Carlyle, both of them great writers and profound thinkers, both of them synthesisers who tried to reconcile scientific truth with religious vision, both of them destined to be pushed aside by a younger generation of impatient fact-finders.

Lovell takes his title from Thomas Carlyle's "Sartor Resartus". Man, according to Carlyle, "sees and fashions for himself a Universe, with azure Starry Spaces, and long Thousands of Years. . . as it were, swathed in, and inextricably over-shrouded; yet it is sky-woven and worthy of a God. Stands he not thereby in the centre of Immensities, in the conflux of Eternities?" If Lovell's book succeeds in persuading a new generation of readers to look at the Universe through the eyes of Thomas Carlyle, it will have done us all a great service. □

Freeman J. Dyson is Professor of Physics at the Institute for Advanced Study, Princeton, New Jersey.

How physicists understand matter

Gerald Feinberg

The Forces of Nature. By P. C. W. Davies. Pp. 231. (Cambridge University Press: Cambridge and New York, 1979.) Hardback £12; paperback £4.25.

PAUL DAVIES is a mathematical physicist with both interest and talent in writing about modern physics for non-specialists. His previous works in this genre include *Space and Time in the Modern Universe* and *The Physics of Time Asymmetry*. There he treated aspects of relativity, thermodynamics and cosmology. In his present volume, *The Forces of Nature*, Davies turns to the central concern of twentieth-century physics, the structure of matter, and the interactions (forces) acting among subatomic particles. The book uses relatively little mathematics, and, in most places, requires no previous knowledge of physics on the readers' part. The result is a broad and usually clear survey of the ways in which physicists now understand matter. However, *The Forces of Nature* is missing a certain spark that was present in Davies' previous books. Also, it is somewhat marred by a number of inaccurate or misleading statements. These do not distort the main thrust of what Davies is doing, but they do make his treatment of some subjects unreliable. As the book does not try to present original contributions to physics, it is style, clarity and accuracy that are of greatest importance, and I will concentrate this review on these questions.

As might be expected from an author whose own research is highly mathematical, *The Forces of Nature* is very much a theorist's book. The ideas of physics are described in detail, but the experimental methods that led to these ideas are given perfunctory treatment. This is especially true of experiments carried out over the past thirty years. I cannot help thinking that this disparity in the treatment of theory and experiment will give readers a distorted view of how physics has developed in the past, and how it may proceed in the future.

The Forces of Nature begins with a brief introduction to Newtonian mechanics, and to electrical, magnetic and gravitational forces. The discussion of the forces is very clear and precise, but that of mechanics is less so. In particular, the description of energy is so vague that a reader will have trouble knowing what the concept means. This introductory chapter concludes with a section on special

relativity theory.

In his next chapter, Davies outlines the quantum theory of atomic structure as developed between 1900 and 1930. The essential feature of such an exposition is its treatment of quantum mechanics, perhaps the major intellectual achievement of the twentieth century. Davies approaches quantum mechanics through its wave aspect, which he explains very well, using analogies with musical instruments. He uses this discussion to indicate why electrons in an atom have discrete energy levels. However, the correct way of describing electrons in an atom, through the notion of a quantum state characterised by definite values of energy, angular momentum and spin, is not introduced clearly. As a result, Davies' discussion of the Pauli exclusion principle is vaguer than it need be. Furthermore, the distinction between fermions and bosons is described in such a way that one of the great achievements of quantum field theory, the connection between spin and statistics, seems a tautology. These problems could have been avoided with only a little more care.

Davies turns next to nuclear structure, and discusses the constituents of nuclei, nuclear stability, and alpha and beta radioactivity. These subjects, especially nuclear stability, are treated well. The description of beta radioactivity, with its distinction between neutrinos emitted in electron capture and antineutrinos emitted in neutron decay, leads into a discussion of antiparticles in general. Here Davies uses the Dirac hole theory, with its heavy reliance on the exclusion principle. This approach has some virtue in making the existence of positrons plausible, but it has two decisive disadvantages. One, mentioned as an afterthought by Davies, is that the hole theory does not apply to bosons, such as charged pions, which also have antiparticles. The other is that the hole theory obscures the fundamental symmetry between particles and antiparticles by making antiparticles seem like interlopers in a Universe composed of particles. That picture is, however, false, and the observed surplus of electrons over positrons, and of protons over antiprotons, is actually an empirical fact that needs explanation, which physicists are beginning to find in the early Universe. Although the hole theory did lead Dirac to predict antiparticles, it has probably outlived its usefulness and should be retired to the same honoured resting place for outmoded physical concepts as Maxwell's mechanical models of electromagnetic fields.

The notion of antiparticles next leads Davies to consider particle creation and annihilation, one of the more surprising consequences of the union of quantum mechanics and relativity. Davies approaches this through the use of quantum field theory, again skillfully

using analogies with the behaviour of musical instruments. An emphasis on the field, rather than the particle aspect of relativistic quantum theory is not the rule among physicists today, most of whom think of quantised fields as no more than convenient mathematical tools for the description of interacting particles. Davies has an additional motive in emphasising fields, which is the desire to demystify the abrupt, unanalysable creations and destructions of particles, by treating these processes as more familiar changes in field amplitudes. However, the amplitudes of the fields are also quantised, and also change abruptly when the corresponding particles are created or destroyed. It is therefore no more accurate to think of transitions between states of a quantised field in classical terms than it is to think of transitions between particle states in that way. In both cases, transitions occur in a way that cannot be predicted in advance, although the transition can be measured after it does occur. It is not a difference here that impels us to use quantised fields. Davies does not mention recent work on solitons, and on vacuum excitations, which is a more basic effort to make the field aspect of relativistic quantum theory play a role separate from the particle aspect.

One of the important consequences of quantum field theory is the notion of virtual particles, and their effect on the properties of 'real' particles. Any existing configuration of particles spends part of its time in other states, which may consist of any combination of particles with the same value of conserved quantities, such as charge, as the original configuration. Davies gives a mostly clear exposition of this idea, both for the electromagnetic field, and for the fields associated with pi mesons. Along the way, he introduces the Feynman diagrams that are now universally used by physicists to symbolise various creation and annihilation processes. However, Davies does overstate the significance of virtual particles in one respect, when he says that the real particles produced in various collision processes are simply the virtual particles already present in the projectile and target. This picture is only true for special cases, such as the emission of very low energy photons in a collision between charges. It is not true for the production of high energy particles in collisions, in which case some of the emerging particles must be imagined to have been created in the collision process itself. William Blake's vision of "a World in a grain of sand" may be qualitatively satisfied by the existence of virtual particles, but it should not be taken as quantitatively sound.

The subject of the next section of *The Forces of Nature* is the profusion of subatomic particles discovered in recent years, and the phenomena of strong and weak interactions that they undergo. This description is fairly thorough and easy to

follow. One important part of the theory of subatomic particles treated in this section is the set of symmetry principles that these interactions satisfy. Davies' discussion of the basis of these principles is curiously Aristotelian, relying on the invariance properties of empty space. Although he is able to draw correct conclusions from this analysis, past experience should make us cautious about the extent to which such a style of argument can be trusted. It would be just as easy to infer Aristotle's form of inertia as Galileo's form from Davies' arguments.

The final section of *The Forces of Nature* deals with recent developments, such as the quark theory of hadrons, and the unified theories of weak and electromagnetic interactions. The discussion here is very up-to-date, and includes the discovery of the upsilon

meson, and of parity non-conservation in deep inelastic electron scattering. There are also nice discussions of spontaneous symmetry breaking and of some reasons why quarks may not be observable. Once again, some things in the text are misstated, such as the mechanism by which charged pion decay occurs in the quark model.

A general stylistic objection to the book is that over and over again Davies resorts to the phrase "it can be shown," or the like, a device that will probably annoy others as much as it does this reviewer. But on the whole, *The Forcers of Nature* is a considerable achievement in popular science writing. It is most likely to appeal to readers with an abstract turn of mind, who like deductive reconstructions of physical phenomena. □

Gerald Feinberg is a Professor of Physics at Columbia University, New York.

Einstein's ideals

Eugene Wigner

Albert Einstein, *The Human Side: New Glimpses from His Archives*. Selected and edited by Helen Dukas and Banesh Hoffman. Pp.168. (Princeton University Press: Princeton, New Jersey, and Guildford, UK, 1979.) \$10; £4.95.

THE purpose of this book is to acquaint the reader with Einstein's social ideas, with his emotional life, with his convictions concerning the objectives man should strive for. And he surely abided by the ideals he put forward in his letters as well as any person could. The book is almost completely restricted to these aspects and contains hardly any information about Einstein's scientific accomplishments. It deals with what the authors call the human side.

As far as Einstein's own direct contributions to the book are concerned, these are almost completely restricted to letters which he sent out and a few which he drafted but did not send off. It does contain also two vitae — one written when he was 17, the other when he was a member of the Prussian Academy of Sciences, in Berlin at the age of 53 — and these are interesting to compare. Most of the rest of the book is due to two of his admirers: his almost life-long secretary Helen Dukas and his past friend and collaborator Banesh Hoffmann. They call themselves Selectors and Editors of the letter collection, but their contribution is actually much greater. It includes also the description of Einstein's relationship to the addressee of the letter, Einstein's attitude towards him or her, the motives leading Einstein to write the letter and the

circumstances under which it was written. All this is done very clearly. They have also written a very nice introduction to the book.

Most of Einstein's letters were originally written in German and some were sent in that language. Others were drafted in German then translated into English by Einstein himself, but in some cases only the original German draft is available. In both these cases translations have been made by the Selectors and Editors, and in some cases this has been a difficult task. A particularly difficult case is that of the poems written by Einstein for inclusion in the letter. But whenever the letter's English formulation was not by Einstein himself, the German original is reproduced in the second part of the book ("German Originals", pp. 119-163). In a few cases, one must admit, the translation is less lively than the original, but it is good even in these cases.

The book does give the reader a vivid impression of the breadth of Einstein's interests, of his modesty and desire to help his fellow men and please them, of his convictions about what is good and what is evil. As to the first question, even the writer of this review, though he knew Einstein since about 1925, was not aware of all his interests. Besides all branches of physics, it also included music — his favourite composers were Bach and Mozart but he did have an affectionate regard for some of the later ones. His love of his violin was well-known to all his acquaintances. But in addition to these well-known interests, he showed great fondness towards the great philosophers of the past, and many of his letters are enlivened by philosophical remarks which give pleasure to the interested reader of the book and must have given even more pleasure to the original recipient of the letter. "The concept of a soul without a body seems to me empty". "What I see in Nature is a magnificent structure that we

Just Published . . .

LORD KELVIN: The Dynamic Victorian

by Harold & Tiby Sharlin

Lord Kelvin (1824-1907) meets no simple definition of scientist-engineer. The reader of this biography will be introduced to an extraordinary figure of a past era who in no way fits the image of the modern specialist. Kelvin was the nonpareil scientist of the 19th century, and his biography encompasses the dynamic scientific changes of the Victorian age. 340 p., 28 ill., £9.60

Also Forthcoming . . .

CLOUDS AND STORMS: The Behavior and Effect of Water in the Atmosphere

by F. H. Ludlam

A reference and text for all atmospheric scientists and scholars in related fields. 500 p., 282 ill., £35.00

PENN STATE UNIVERSITY PRESS

1 Gower Street, London WC1
Telephone (01) 580 3994

Circle No. 61 on Reader Enquiry Card.

BIO-MATHEMATICS

Revue de Bio-Mathématique.

Founded in 1962.
4 issues per year.

Bilingual English-French

If direct application of mathematics to biology interests you, if you think that concepts such as Form, Structure, Complexity of living organisms are worth of putting into mathematical language, or that the concept of Entropy and Information may play an important part in the evolution of the living world, "Bio-Mathematics" will give you something to think about.

A list of published papers is available.

Editions Européennes
Il bis Avenue
de la Providence
92160 Antony, France.

Subscription 72F.

Circle No. 60 on Reader Enquiry Card.

can comprehend only very imperfectly, and that must fill a thinking person with a feeling of humility" (pp 39 and 40) are two such passages. But there are many, and even if one does not fully agree with them, all are refreshing. He also defended philosophy in general against its deprecators even when recognising its weakness: "Philosophy is like a mother who gave birth and endowed all other sciences" (p106) is perhaps an exaggeration but a well-meant one.

Einstein's love of poesis is also little recognised. He even wrote some poems, all of a slightly humorous nature, for his letters. About ten of these are contained in the book, and all are amusing.

Einstein's attitude towards religion is also clearly expressed in his letters. He felt — as many people do today — that its main role should be in the ethical domain, whereas its cognitive assertions should be more in the background. He also writes a good deal about the extinction of life — one must, with sadness, come to the conclusion that he enjoyed his last few years very little and considered the extinction of his life not only cognitively, but to some degree also emotionally, as a liberation from obligations.

Einstein's political convictions are also very apparent from his letters. These are, of course, generally known: he was opposed to all dictatorships, be they of the national socialistic — that is, Hitler-inspired and anti-semitic — or of communistic nature. In fact, one draft letter (pp110-112) is so vehement that it was not sent out but, according to the introduction preceding it, "must have brought him a feeling of relief".

The preceding discussion contains, of course, only a superficial review of the kind of information the reader will gain about Einstein's interests and thinking when reading this book. And the information will appear in a much more lively fashion than the foregoing summary presents it.

The book contains more than a hundred letters. To whom were they addressed? A few to his sister, Maja, a few more to his earliest physicist friends Zangger, Ehrenfest and Lanczos, but even more, about eight, to his psychiatrist friend Juliusburger. There is no letter to either of his wives or to the rest of his family. The rest of the letters are practically all answers to letters he received, each from a different person. With about half of these he had some acquaintance, the other's being written to please or comfort people he had not heard of before. Many of these letters, the writing of which was stimulated by kindness or compassion, contain passages which are truly memorable, and manifest deep insights. A few of the other letters are directed to editors of journals and about four to ministers of churches. These latter all have a strong political undertone.

It is not clear how the letters published were selected, nor is it clear how Einstein had chosen the letters to be answered. In

one of his letters (p43) he praises the one which he answers as being very reasonable, in contrast to the hundreds of other letters which he was receiving, most of which, of course, he did not answer. It would also be interesting to know where and how the letters and the drafts of the letters published were found.

The English language part of the book (the first 115 pages) are arranged into 12 sections. These sections, however, have no titles and it is not clear on what basis the various letters are distributed into these sections. This has advantages if one reads the book from cover to cover — it is not easy to digest 10 philosophical letters in succession and not refreshing to read several complaints about politicians' misdeeds one after the other. But if one wants to recover a passage which one remembers vaguely, it would be good to have either a definite order of the articles in the book, or at least an index at the end of it. Similarly, the time ordering of the letters seems to be a

random one. Thus, Section 6 (pp54-74) has articles dating from '33, then '51 and '53, then '27, again '33, '35, '21, and so on, ending up with one of '27. The subjects vary equally greatly, the first is political, the next a thank-you for the offer of financial help, the next refers to physics, then comes a letter to a student publication, then a praise of science in general and so it goes on. It is amusing to read all this, but a catalogue surely would be useful.

After all this criticism, let me compliment again the Selectors and Editors for the very good job they have done. It surely required not only knowledge but also devotion to the job and a true interest in the human side of Einstein. □

Eugene Wigner first met Einstein in 1925, while a student in Berlin. He had closer contact with him after 1933 when both lived in Princeton, New Jersey.

The quantum and its supporting planks

P.T. Landsberg

Black-Body Theory and the Quantum Discontinuity, 1894-1912. By T.S. Kuhn. Pp. 512. (Clarendon/Oxford University Press: Oxford and New York, 1978.) £12.

THE realisation that discontinuities (or quanta of energy) are needed for the description of microscopic phenomena represented one of the great transformations of human thought. Not that everything was believed to be continuous before that — the atomic concept of Democritus, the distinct notes of musical instruments, comets and explosions had been part of the intellectual furniture for centuries, and they certainly implied discontinuities of sorts. But they were not fundamental. Comets continued to be, when not in view; explosions could presumably be analysed into a more or less continuous sequence of chemical reactions; musical notes could be changed by altering the tension in the wire; and the constitution of atoms (if they existed, one would add in 1900) posed in any case intractable problems, for example, how could they be indivisible if they participated in the production of spectral lines? Indeed, as W.K. Clifford observed, an atom must be at least as complicated as a grand piano. Upon this placid scene, in which physics seemed to be approaching a completed structure, there floated gently (for it did not 'burst') Planck's theory of

the energy density, as a function of frequency, of radiation when in thermal equilibrium with bodies at temperature T (black-body radiation). Shortly afterwards arose the problems of relativity, specific heat anomalies, etc., and so black-body radiation never lost the charisma of having been the first problem area which brought deep changes to classical physics. It did so by suggesting that an atom oscillating linearly at a frequency ν has available only discrete energies $h\nu, 2h\nu, \dots$ and so on, whereas classical theory would have allowed a continuous range of energies. Here h is the newly introduced constant of nature, now called Planck's constant.

At precisely what time and through whose pen did these discontinuities enter physics? The normal answer is that the year was 1900 and the man was Max Planck. In this scholarly study, which can boast 90 pages of notes and references, Kuhn suggests an amendment. Planck restricted the energy of N oscillators to be integral multiples of an energy unit, ϵ say, a type of "quantisation" already envisaged by Boltzmann in 1877, but he did not impose this constraint on a single oscillator until after 1906 (see p126), the year in which this requirement had been emphasised independently by Paul Ehrenfest and Einstein, "the two physicists who first recognised that Planck's black-body law could not be derived without restricting resonator energy to integral multiples of h or some equivalent non-classical step" (page ix).

In the Epilogue Kuhn discusses Planck's "second theory" of heat radiation (1911) which introduced the notion that the mean energy of an atomic oscillator goes to a constant and non-zero value at the lowest temperatures. Although this zero-point energy remained important, Planck's second theory was

also to suffer profound amendments. By now, as Kuhn shows, the scientific community was turning to the quantum theory of specific heats.

Scientific community? In those far off days of the first Davis Cup matches, of Henry Ford and Thomas Mann, the number of authors who wrote on black-body theory did not exceed 20 even by 1914. By that time there were still only about sixty-five authors who wrote on the quantum theory, but the number was rapidly rising (as clear from the only three figures in the book). Does today's science harbour another growth point of this significance so that mathematically simple but conceptually gigantic leaps can again be made? Those who doubt that such a growth point can still be found in physics hope, like drowning men clutching at a straw, that it is perhaps still possible in biology. It is, however, a delight of science that there could yet be hope for physics. Who knows?

Mathematics is not popular with readers of book reviews, but to understand the background of Planck's arguments a gentle sniff of three results is needed. First, as black-body radiation does not depend on the material systems with which it is in contact (Kirchhoff, 1860), the simplest systems can be chosen. These are oscillators, N in number say for each frequency ν . The mean energy $U(\nu, T)$ of one of them is then simply related to the energy density $q(\nu, T)$ of the radiation (Planck, 1899). Secondly, thermodynamics tells us how to find the mean entropy $S(U)$ of an oscillator in terms of U , provided $U(\nu, T)$ is known. (Example: if $U = kT$, then $dS/dU = 1/T = k/U$, so $S = k \ln U$.) Thirdly, if one has a fundamental model to calculate the number W of so-called microstates of a system one can evaluate the entropy with the aid of a simple relation (Boltzmann 1877).

Now a remark about three Planck papers. In March 1900 he injected an empirical formula for q due to Wien (1896) into this theoretical structure, and went from q to U to S . But then he could only check certain properties of S and nothing revolutionary resulted. In October 1900 he injected into the same structure a new (S, U) -relationship which contained the classical result $d^2S/dU^2 = -k/U^2$ and the Wien result $d^2S/dU^2 = -A/U$ as limits. It was a trial, or interpolation formula, and, passing in the opposite direction now, he inferred U and q . The latter result was what has since become known as the famous Planck distribution law. "Permit me to direct your attention to this new formula" says Planck, "... I consider it to be the simplest apart from Wien's." But I had no firm basis in theory! Planck tells us that he worked very hard to find such a basis and on 14 December 1900, he produced a W -expression from the mechanics of oscillators. This is where he was very brief and not very clear. In any case, he now proceeded in the accepted

logical direction from W to S to U and q , and that was the essential job done. Or was it?

The problem for the studious reader, 75 years later, is: how did he get W ? He says about the total energy of the N oscillators (we suppress the suffix ν , as we consider a given frequency), that "it is necessary" that it shall be considered to be "not a continuous, infinitely divisible quantity", but that "it shall be considered to be discrete and to consist of a finite number of equal magnitudes" (*Ann. Phys.* 2, 4, 553; January, 1901), "which is the most essential point of the whole calculation" (*Verh. d. Dtsch. Phys. Ges.*, 2, 237; December, 1900).

Kuhn unfortunately does not quote these passages, and argues that the fact that the total N -oscillator energy E_N is an integer n multiplied by an energy unit ϵ does not give the essence of the discontinuity: "If quantization is the subdivision of total energy into finite parts, then Boltzmann is its author" (p127). This is a possible point of view. An alternative, more generous, interpretation is to recall, first, that the oscillators are assumed far enough apart not to interact with each other. Hence, if one adds a single oscillator, then its average energy $E_1 = U$ must be the difference between the two Planckian results $E_{N+1} - E_N = n\epsilon - m\epsilon$ where n and m are integers. Hence Planck's result extends to $U = r\epsilon$ ($r = 1, 2, \dots$). Secondly, what was still a fictitious model for Boltzmann, who after all took the limits $\epsilon \rightarrow N \rightarrow \infty$, had become physically relevant in Planck's hands. Nevertheless, it is certainly true that Planck's reticence is puzzling, as has been pointed out (for example, by M.J. Klein, *Paul Ehrenfest*, Vol I, p228, North-Holland: Amsterdam, 1970; by H.-G. Schöpf, *Von Kirchhoff bis Planck*, p106, Akademie: Berlin, 1978). Although there will therefore be discussions among historians of science sparked off by this book, we shall never know exactly what was in Planck's mind in 1900, nor is it very important to know. It strikes me that Planck knew the chain $q - U - S - W$ very well and had great confidence in his q ; so he worked backwards to find the W needed. Perhaps it was because Boltzmann had done much of the mathematics needed by Planck that Planck did not expound the theory of the W as clearly as he might have done. That there existed a sensible expression at all was to him, and rightly, an achievement. To infer single oscillator quantisation (which he might have done by the argument given above) was in 1900 against his wish, as he did not want to leave classical physics, as Kuhn reminds us again so clearly. In any case should an average oscillator energy be quantised? Surely not, a point apparently missed by some later commentators.

As to Einstein, he emerges as hardly ever wrong, as the following story shows. On 12 June 1913, Planck, Nernst,

M

**THE
MACMILLAN
DICTIONARY
OF
ASTRONOMY
VALERIE
ILLINGWORTH**

- * Hundreds of references from AAT to the Zurich relative sunspot number
- * Complete and up-to-date. All the most recent discoveries and theories covered.
- * Fully cross-referenced
- * Illustrations, tables and diagrams

The ideal personal reference for both the specialist and the interested layman.

£8.95 0 333 232631

For further details contact The Publicity Dept., 4 Little Essex Street, London WC2 3LF.

M MACMILLAN PRESS

Sorry, for copyright reasons some images on this page may not be available online

Rubens and Warburg proposed Einstein for full membership of the Prussian Academy of Sciences, describing the achievements of the 34-year-old scientist in glowing terms. From the point of view of the book under review it is of interest that they did, however, remark: "That he has occasionally missed the target in his speculations, as for instance in his light quantum hypothesis, is not something that should count too severely against him; for even in the most exact of sciences it is not possible to introduce real advances without occasionally taking a risk". One can almost hear Planck's voice. It is a sobering thought for those called upon to judge the work of their peers in scientific academies, research committees, book reviews and promotion boards that this distinguished group of four was so devastatingly wrong; after all the light quantum hypothesis was essential to Einstein's explanation of the photoelectric effect which was to be cited by the Nobel Committee in 1921. This interesting

matter did not escape Kuhn's eagle eye (though he attributes it to 1914) but he notes it only in passing (p182). Yet there it is. The careful and conservative Planck held back. Friend and supporter of Einstein's though he was - to the extent of risking the concentration camp by his 1933 declaration in support of Einstein - the photon picture of radiation was too much in advance of current thinking in 1905.

My main criticism of this fine book — so lovingly researched as to include abstracts, reviews and relevant citations of some of the key papers — is that this very detail has prevented a tight organisation of the material and of the author's conclusions, which are therefore somewhat buried at various points, in spite of a good index. The Epilogue might have included a two- or three-page forward look into the 1920s, for reasons which will be touched on below.

An alert reader may ask a question, to which the book does not supply an

answer, as to whether systems other than oscillators, for example rotators, were studied in contact with black-body radiation. If not, why not? In any case, the element of confusion between E_N and E_1 and between quantising $E_1 = U$ as against quantising the unaveraged single oscillator energy, means that the Planck argument has to be replaced. By treating radiation as a gas of "light quanta" and introducing the notion of indistinguishability of quanta of given energy, Bose (1924) gave an argument which no longer depended on any parameters of the material system in contact with the radiation. In a modern exposition Bose's W had the same form as Planck's, $W = (N + P - 1)!/P!(N - 1)!$. However, Planck oscillator number N became the number of states in a typical narrow energy range of the quanta considered, and Planck's integer $P = E_N/\epsilon$ became the number of quanta to be distributed over these states in an optimal manner. (For Planck P was the number of discrete energy elements to be distributed over the N oscillators). Although this was much more satisfactory, the result was approximate (Stirling's approximation). On the whole this does not worry people. However, one cannot conceal that this approximation breaks down for the small number of quanta which can be found in high energies, and I found (1954) that if the Stirling approximation is improved one gets into trouble. The Planck law *can* be derived as an exact result, but as far as I know only by using the grand canonical ensemble or by taking a limit.

Two queries may be in order in conclusion. In "overblowing" a wind instrument the note jumps as a higher mode is excited. This is typical of *classical* discontinuities. They are not mentioned in the book but it would be of interest to study them, together with Schrödinger's and Planck's approaches, in a historical context. Secondly, the case studied here suggests (though one must not generalise from one example) that a great scientific advance — a revolution if you like — tends to dissolve into little steps on closer inspection. The same man may take different steps at different times, so that he may in the end have made a major contribution; but small steps they are nevertheless. If this is a general rule, with a few exceptions such as general relativity, it would be interesting to hear Kuhn, the author of the *Structure of Scientific Revolutions* (1962) consider it in the light of this latest book. The topic itself has been much discussed of course (for example, by S. Toulmin, *Human Understanding*, Vol. 1, 1972), but it is particularly interesting in connection with the story of black-body radiation. □

P. T. Landsberg is Professor of Mathematics at the University of Southampton, UK.

articles

Direct imaging of the twin QSOs 0957 + 561 A and B: the gravitational lens interpretation

Mark T. Adams & Todd A. Boroson

Steward Observatory, University of Arizona, Tucson, Arizona 85721

Recent observations have indicated that the twin quasil stellar objects 0957 + 561 A and B might be images produced by a gravitational lens. New direct observations are presented, including the probable detection of an object between the two quasil stellar objects. The implications of these observations for the nature of the twin quasil stellar objects are discussed.

WALSH *ET AL.*¹ have recently announced the discovery of a pair of quasil stellar objects (QSOs) that are separated by 5.7 arc s and that have the same emission redshift, 1.405. These QSOs, 0957 + 561 A and B, were found to have several similarities. The redshifts of the C IV λ 1,549 and C III] λ 1,909 emission lines are significantly different in each QSO but identical to the accuracy of measurement between the two objects. The equivalent widths of these two lines are, respectively, the same in the two QSOs. Furthermore, a strong low- Δz absorption system at approximately the same redshift was seen in the spectrum of each object. Subsequent spectroscopic observations at the Multiple Mirror Telescope by Weymann *et al.*² revealed that the redshifts of the absorption systems in the two QSOs differed by $7 \pm 15 \text{ km s}^{-1}$. The amazing similarities between these two objects have led to speculations^{1,2} that the image of a single QSO was being split by a gravitational lens in the line of sight, and to crude calculations of the parameters necessary to produce such an effect.

The large mass implied by these calculations ($\sim 10^{13} M_{\odot}$) led us to believe that if such an object existed and was a particularly massive galaxy, it should be visible on a suitably deep, direct picture of the region. Also, because the images formed by a gravitational lens are not expected to be circular, it might be instructive to examine the size and shape of the images of the QSOs in such a picture.

Observations

The two QSOs were observed on 15 June 1979 with the Kitt Peak National Observatory (KPNO) 4-m telescope and the ISIT video camera. Four 13.6-min. integrations were obtained

through an *R* filter. The resulting field in this configuration is ~ 75 arc s on a side; each pixel is ~ 0.29 arc s. The seeing was estimated at the telescope to be 2 arc s. Basic reduction of the data included subtraction of a dark frame and division of the object field by a flat-field exposure obtained through the same filter.

These four frames were inspected using the KPNO interactive picture processing system (IPPS). This inspection revealed that the quality of the images in the last exposure was significantly poorer than in the other three due to deterioration of the seeing at high air mass (sec $z \sim 2.2$).

In each of the first three frames the centre of gravity of each QSO image was determined. These centres agree to ≤ 1 pixel frame-to-frame. An equal weight average of these three exposures was then calculated and used for all subsequent measurements. This final picture is shown in Fig. 1.

Analysis

Several different types of measurements were made using the IPPS surface brightness routines written by Strom³.

Simulated aperture photometry of the two QSOs in our averaged frame provides a scale factor for conversion of our arbitrary intensity units into *R* magnitudes. The adopted *R* magnitudes for the two QSOs were taken from Walsh *et al.*¹. The determined relationship is $m_R = -2.5 \log I + 30.6$, where *I* is the total intensity within the aperture. Magnitudes obtained in this manner are probably accurate to ± 0.5 .

We attempted to detect or set an upper limit to any excess flux present between the two QSOs. First, an average value for the sky was determined by sampling several blank areas adjacent to the QSOs. A sky surface brightness of $20.5 \text{ mag arc s}^{-2}$ in *R* was measured. Next, the contribution of each QSO to the point midway between them was determined. The flux in a series of 1.16 arc s circular apertures, arranged as shown in Fig. 2, was measured. The radius of each semicircle is equal to half the separation of the two QSOs. This procedure was used to estimate the possible error due to asymmetric images.

This possibility has important implications for the significance of a detection. If we find that the standard deviation of the measurements among the apertures is less than or equal to that expected from measurement uncertainties (for example, photon

statistics, flat-field and dark-count uncertainties, nonlinearity in the detector), we can justify using the standard deviation of the mean as an estimate of the accuracy. If, however, the variation among the apertures around the QSOs is larger than that expected from measurement uncertainties, we must conclude that our apertures are sampling a variety of values, and in this case the standard deviation of a single aperture is a better estimate of the accuracy.

Unfortunately, the results of this comparison are somewhat ambiguous. Measurement uncertainties were determined by sampling the sky in a series of adjacent apertures, yielding a variation of ~1%. Around QSO A, the standard deviation of the measurements exceeds that expected by ~45%. A χ^2 test indicates a 15% probability of a distribution as unfavourable as that observed arising from the expected gaussian distribution. Around QSO B, the standard deviation is almost twice that predicted by measurement errors. The variation in this case, however, seems to be systematic in that the four apertures most nearly along the line perpendicular to the separation of the two QSOs are much higher than the other four. The most likely explanation of this asymmetry is that we have marginally resolved QSO B in the perpendicular direction.

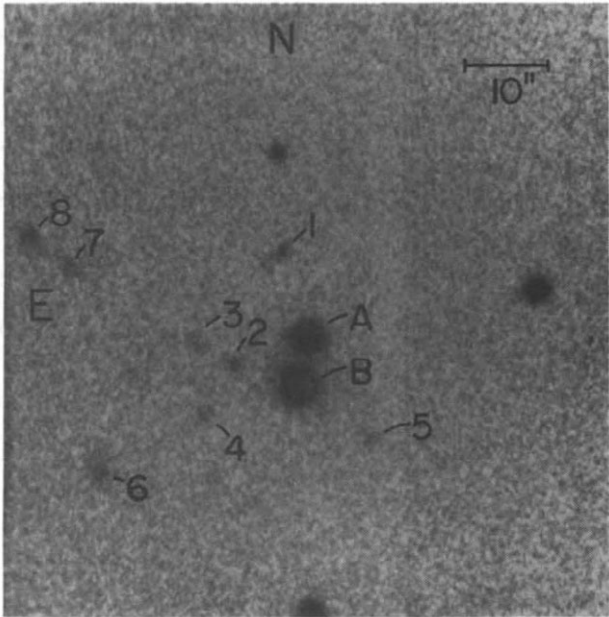


Fig. 1 The final averaged *R*-band picture of the region surrounding 0957 + 561 A and B. The eight galaxies listed in Table 2 are indicated.

Because of the difficulty in ascertaining which types of errors dominate, we will consider two cases. The flux measurements for each case are presented in Table 1. In case 1 we consider the variation around QSO A to be statistical. For QSO B, we use only the four apertures most nearly along the line of separation and consider the variation among them to be statistical. In case 2 we consider all variations to be real and, therefore, use all points in the mean; the quoted errors are the standard deviation of a single measurement. Case 1 indicates a 5.4 σ detection which corresponds to $m_R = 23.1$; case 2 indicates a 2.0 σ detection which corresponds to $m_R = 23.4$.

Visual examination of our data suggested that the image of QSO B is larger than that of QSO A. To quantify this we measured the radial profiles of the two QSOs perpendicular to their separation. Since the central surface brightness of QSO B

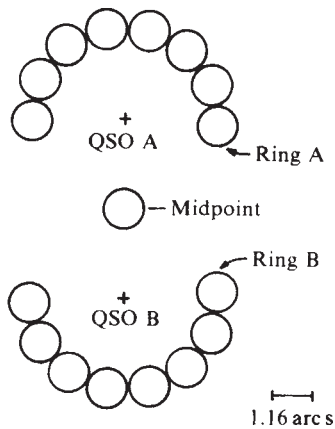


Fig. 2. The geometric configuration used in the photometric measurements.

is ~12% lower than that of QSO A, we scaled up the measurements of QSO B by this amount before comparing them with QSO A. The resulting profiles (Fig. 3) clearly show that at low surface brightness QSO B is ~10% broader than QSO A.

We measured the magnitudes of eight faint nonstellar objects in the field. These measurements were obtained through (1) a 1.16-arc s aperture for comparison with our midpoint photometry; and (2) a 6.44-arc s aperture which should contain essentially all the light of each galaxy (Table 2). The galaxy designations are shown in Fig. 1.

Discussion

Two ways of qualitatively accounting for the original observations have been proposed. The first hypothesis is that the two objects are separate QSOs that, by chance or environment, have evolved with remarkably similar characteristics. This hypothesis requires that almost identical absorbing clouds are found in the line of sight to both QSOs at precisely the same redshift. The second interpretation involves a single QSO whose image has been split by a gravitational lens.

To discuss the gravitational lens hypothesis more quantitatively, we begin by calculating the expected characteristics of the lens object. This calculation involves the following three assumptions. (1) The object is a galaxy with a velocity dispersion given by

$$[\sigma \text{ (km s}^{-1}\text{)}]^2 = \frac{106,875 (1 + z_L) [(1 + z_Q)^2 - 1]}{[(1 + z_Q)^2 - (1 + z_L)^2]} \tag{1}$$

where z_L is the redshift of the lens, z_Q is the redshift of the QSO. This formula is derived from equation (1) of Weyman *et al.*² using their values of θ_{sep} and n . The mass is derived from this by assuming that the galaxy is an isothermal sphere.

Table 1 Excess flux measurements		
	Case 1 Measurement error	Case 2 Real variation
Ring A	798.0 ± 66.6	798.0 ± 188.5
Ring B	1,115.9 ± 62.8	1,360.9 ± 291.5
Midpoint	2,904.1 ± 158.3	2,904.1 ± 158.3
Excess	990.2 ± 184.7	745.2 ± 382.0

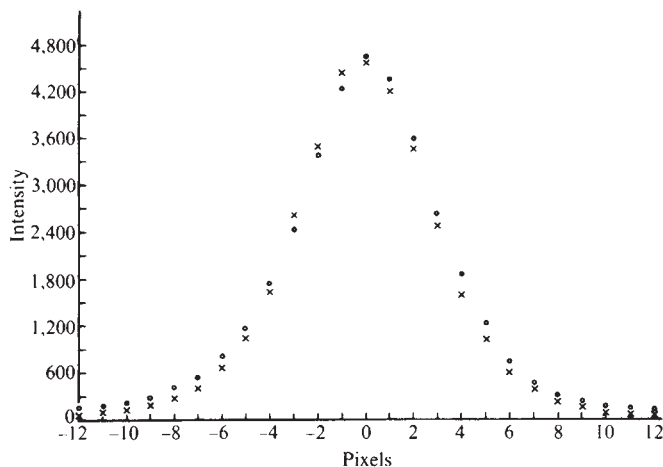


Fig. 3 Profiles of the two QSOs ($\times$, QSO A; $\circ$, QSO B) in the direction perpendicular to their separation. The intensities have been normalised to the central three pixels of QSO A.

(2) As the mass-to-light ratios M/L for galaxies are poorly determined, we have done the calculation for two cases: $M/L = 5$ and $M/L = 30$ in solar units.

(3) $H_0 = 50 \text{ km s}^{-1} \text{ Mpc}^{-1}$ and $q_0 = 0$. Table 3 lists, for various possible z_L values, the absolute R magnitude of the lens galaxy, M_R , the total apparent R magnitude of the lens galaxy, m_T , and the expected R magnitude through a 1.16-arc s diameter aperture m_{ap} . R -band K corrections were extrapolated from the published V -band K corrections of Pence⁴. The magnitude difference between m_T and m_{ap} was calculated from the M87 surface photometry of Young *et al.*⁵ by comparing the flux in the small aperture with that in a 6 arc s aperture at each redshift. The resulting magnitudes in Table 3 are very uncertain, primarily due to the K corrections and luminosity evolution which we have ignored. Moreover, comparison of our measured magnitude with the numbers in Table 3 is hindered by uncertainty in the absolute calibration and ignorance of the correct M/L . Thus differences of up to 1 mag in this comparison are within the possible range of error.

The possible interpretations of our detection of an $m_R = 23.1$ object between the two QSO images are: (1) the object could be the lens galaxy; (2) the object could be a faint field galaxy in the line of sight; (3) the object could be the galaxy responsible for the absorption system.

If the detected object is the lens galaxy, it can be seen from Table 3 that it must be located at very nearly the QSO redshift, or it must have a large M/L . The extended profile of QSO B may argue for the validity of the lens interpretation. If the lens is circular and slightly out of the line of sight, it is expected that the two images will not be identical. The image further from the lens will be brighter and more elongated perpendicular to the separation of the images⁶. Note that QSO B has a redder

continuum than QSO A¹. If this is indicative of greater extinction, then QSO B is the brighter of the two.

The other two interpretations of the nature of the object between the QSO images argue for the 'non-lens' picture. The explanation that the object is a field galaxy located by chance in the line of sight is unlikely because of the probability of finding a galaxy brighter than 23.1 mag in a 1.16-arc s aperture. Using the faint galaxy counts of Tyson and Jarvis⁷, we estimate that the likelihood of this is $< 10^{-3}$. These counts and the work of Kron⁸ indicate that the expected number of galaxies visible in our field is ~ 3 –5, and thus it is unlikely that the eight galaxies seen are associated with a rich cluster.

The third possibility, that the object is the galaxy responsible for the absorption in the two QSOs 65 kpc apart, cannot be ruled out by this statistical argument. However, the primary argument against this explanation is the very large luminosity required for the absorbing galaxy. Even in the optimistic M/L case, the necessary luminosity requires that $M_V < -26$. This seems unlikely, considering the local galaxy luminosity function from which it seems that significant luminosity evolution would be needed to attain such a value. The evidence at this time^{7,8} favours little, if any, luminosity evolution at this magnitude. Also, no QSO with a redshift as large as 1.4 has been detected as nonstellar.

Table 3 Calculated lens characteristics

z	$M/L = 5$			$M/L = 30$		
	$-M_R$	m_T	m_{ap}	$-M_R$	m_T	m_{ap}
0.1	23.2	15.9	17.5	21.3	17.8	19.4
0.2	24.1	16.7	18.0	22.1	18.7	20.0
0.4	24.9	17.9	18.8	22.9	19.9	20.8
0.6	25.4	19.2	19.9	23.5	21.0	21.7
0.8	26.0	20.0	20.7	24.0	22.0	22.7
1.0	26.6	20.4	21.0	24.6	22.4	23.0
1.2	27.4	20.7	21.3	25.5	22.6	23.2

Conclusions

We have obtained a deep R -band picture of the double QSO 0957+561 A and B. We have detected excess flux between the two QSOs which corresponds to $m_R = 23.1$. The significance of this detection strongly depends on the nature of the errors. QSO B was found to have a more extended radial profile than QSO A in the direction perpendicular to their separation.

Both these results can be interpreted as consistent with the two competing hypotheses: a gravitational lens or two distinct QSOs. However, a statistical argument favours the gravitational lens interpretation.

We thank Drs S. Strom, R. Weymann, F. Chaffee, J. Liebert and T. Sargent for helpful discussions and Hal Halbedel for technical assistance. The authors were visiting observers at Kitt Peak National Observatory, operated under contract with the NSF.

Table 2 Field galaxy photometry

No.	m_R	
	(aperture 1.16 arc s)	(aperture 6.44 arc s)
1	22.4	20.9
2	22.6	20.5
3	24.0	22.1
4	23.4	21.3
5	23.5	22.1
6	22.9	20.6
7	22.9	20.8
8	22.3	20.1

Received 18 July; accepted 13 September 1979.

- Walsh, D., Carswell, R. F. & Weymann, R. J. *Nature* **279**, 381 (1979).
- Weymann, R. J. *et al. Astrophys. J. Lett.* (in the press).
- Strom, S. E. & Strom, K. M. *Astr. J.* **83**, 73 (1978).
- Pence, W. *Astrophys. J.* **203**, 39 (1976).
- Young, P. J., Westphal, J. A., Kristian, J., Wilson, C. P. & Landauer, F. P. *Astrophys. J.* **221**, 721 (1978).
- Refsdal, S. *Mon. Not. R. astr. Soc.* **128**, 295 (1964).
- Tyson, J. A. & Jarvis, J. F. *Astrophys. J. Lett.* **230**, L153 (1979).
- Kron, R. thesis, Univ. California, Berkeley (1978).

Oxidation of aerosoled ultrafine iron particles

K. Haneda* & A. H. Morrish

Department of Physics, University of Manitoba, Winnipeg, Manitoba, Canada R3T 2N2

Aerosoled ultrafine iron particles, in the few hundred ångström size range, have been subjected to different oxidation modes. X-ray and Mössbauer techniques have been used to study the morphology of the oxide scales and the diminution of the recoilless fractions and the hyperfine fields.

ULTRAFINE particles of iron are of considerable interest as they form the active component of magnetic tapes now under development by the recording industry. A way of making small metal particles is by an aerosol or evaporation technique developed more than a decade ago¹⁻³. In essence, metals are evaporated in an inert gas atmosphere at reduced pressure. The metallic atoms have a reduced mean-free-path, and eventually condense to form small particles. Particle size can be controlled to some extent by changing the pressure or species of the inert gas.

Very small iron particles are pyrophoric. The oxidation of metallic iron in the form of sheets, foils, or even single crystals has been studied extensively⁴⁻⁷; the motivation has been an interest in corrosion and passivation processes. Little is known about the oxide layers formed on the surface of ultrafine iron particles⁸⁻¹⁰; it is therefore timely and relevant to investigate the oxidation modes for such particles.

Earlier experiments in our laboratory showed the oxide layer to be composed of small crystallites with the spinel structure¹⁰, probably a mixture of Fe_3O_4 and $\gamma\text{-Fe}_2\text{O}_3$. Further, for a sample with particles an average diameter of 238 Å, only a slight Mössbauer absorption was observed at room temperature, whereas at 77 K a well-defined hyperfine-split spectrum was obtained¹¹. Apparently at 300 K most of the particles experience a recoil on absorption of the γ -ray photon. The Debye-Waller factor for small particles has attracted the attention of many researchers, and does not yet seem to be settled¹²⁻¹⁸.

Iron particles can be passivated by an O_2 and N_2 gas mixture low in oxygen content¹⁹, that is, by a slow oxidation. At the other extreme, on exposure to open air even at room temperature, the ultrafine particles glow, indicating that a relatively high temperature is reached. Hence, the chemical and physical properties of ultrafine particles may be different, depending on whether a slow or a fast oxidation is used. This article reports on an X-ray and Mössbauer study of aerosoled iron particles subjected to different extreme oxidation modes. Special attention is given to the morphology of the oxide, the recoilless fraction, and the hyperfine fields.

Oxidation experiments

Five samples of small iron particles in the 200–400 Å range were prepared by evaporation into a 1 to 3 torr helium gas atmos-

phere. They were produced at Osaka University, Japan, and made available through Professor A. Tasaki and Dr M. Takao. The samples labelled A–E were collected in sample containers, and sealed in a helium gas atmosphere.

The oxidation of the samples was achieved in the following way. Sample E was immediately exposed to air, and after completion of the rapid oxidation was quenched and stored in ethyl alcohol. Sample D was suddenly exposed to air about 3 weeks later; it glowed and the powder colour changed rapidly from black to dark brown. Thus, samples D and E were subjected to fast oxidation. Samples A, B and C were oxidised slowly by air entering through a small leak in the seal. Although this slow leak continued over a period of a few weeks, the actual oxidation rates are of course unknown. When samples A, B and C were exposed to air, no further changes occurred, indicating that complete passivation had taken place, as suggested by Tasaki *et al.*²⁰. Indeed, X-ray and Mössbauer data showed that another sample, similar to C, underwent no measurable changes over a 3-year period.

The average particle size of each sample was determined by the Brunauer–Emmett–Teller (BET) nitrogen adsorption method assuming a spherical shape. The results are listed in Table 1.

Table 1 Properties of samples A, B, C, D and E

Sample	Particle size (Å)	Crystallite size (Å) ^c		Composition (%) ^c		Mössbauer absorption 300 K
		Fe	Oxide	Fe	Oxide	
A	380	133	68	18	82	Almost none
B	238	76	51	5	95	A little
C	293	100	27	20	80	A little
D	329		101		≈100	Hyperfine split
E	366		120		≈100	Hyperfine split

* Determined from X-ray line broadening using (311) for cubic oxide and (110) for metallic Fe.

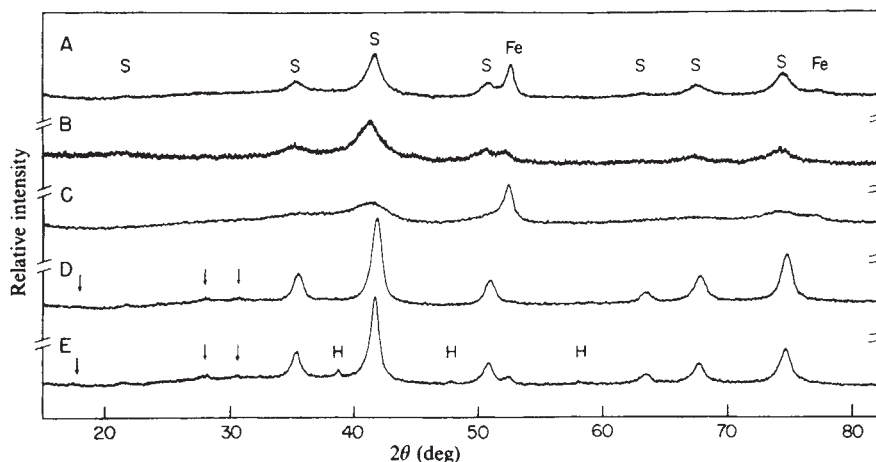
^c Obtained from Mössbauer absorption area.

X-ray measurements

X-ray diffractograms were taken for the five samples using $\text{CoK}\alpha$ radiation; part of the recorder plots is shown in Fig. 1. For slowly oxidised samples (A, B, C) the diffraction profiles indicate two phases—one with the crystal structure of ordinary $\alpha\text{-Fe}$, and the other, constituting a significant fraction, has the structure of spinel iron oxide, either magnetite (Fe_3O_4), $\gamma\text{-Fe}_2\text{O}_3$ or a mixture of both oxides. No line corresponding to $\alpha\text{-Fe}_2\text{O}_3$ (haematite) was detected. Although the superlattice lines peculiar to $\gamma\text{-Fe}_2\text{O}_3$ were not observed, the presence of $\gamma\text{-Fe}_2\text{O}_3$ is not ruled out for the following reasons. First, as shown in our earlier study²¹, the transformation from Fe_3O_4 to $\gamma\text{-Fe}_2\text{O}_3$ takes place with good probability in the small particle region. Second, the vacancy-ordered superstructure lines associated with bulk $\gamma\text{-Fe}_2\text{O}_3$ are reduced or absent in ultrafine particles because then the vacancies, although they exclusively occupy B sites, are

* Permanent address: Research Institute for Scientific Measurements, Tohoku University, Sendai, Japan.

Fig. 1 X-ray diffraction recorder plots for samples A, B, C, D and E. Here 2θ is twice the Bragg angle. S, spinel type iron-oxide phase; Fe, Fe phase; H, α -Fe₂O₃ phase; arrow, vacancy-ordered superlattice line peculiar to γ -Fe₂O₃.



disordered²². Third, every oxide diffraction line for the three samples is slightly shifted to higher angles, that is, towards the γ -Fe₂O₃ and away from the Fe₃O₄ positions. Therefore, the data probably imply that the oxide is a mixture of stoichiometric Fe₃O₄ and γ -Fe₂O₃.

Sample D, oxidised by the fast mode, does exhibit faint vacancy-ordered superlattice X-ray lines. No line of metallic iron or α -Fe₂O₃ was detected. In addition, both the X-ray line positions and the dark brownish colour are close to those associated with γ -Fe₂O₃. It follows that this sample is almost entirely composed of γ -Fe₂O₃.

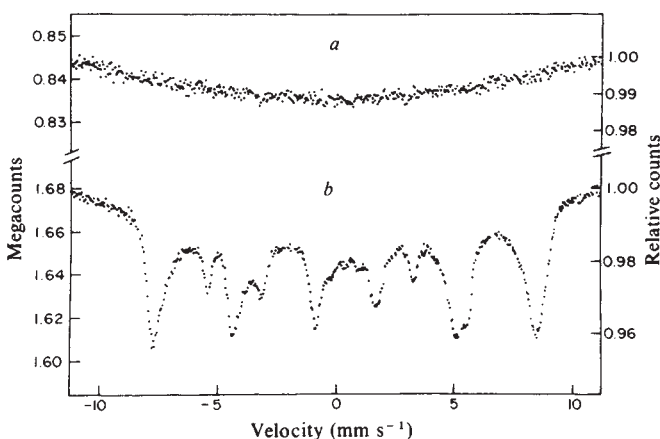


Fig. 2 Mössbauer spectra for aerosoled Fe particles subject to slow oxidation, sample A (380 Å). *a*, At 300 K; *b*, at 77 K.

The pattern for sample E, oxidised quickly then quenched in C₂H₅OH, shows γ -Fe₂O₃ lines, including superlattice ones, as well as low intensity α -Fe₂O₃ and α -Fe lines. The presence of the latter suggests that the oxidation may have been faster for sample E than D, and that the quenching may have been a factor.

The variation in the X-ray linewidths is of particular interest. For samples A, B and C, the spinel lines are much broader than those of iron. In addition, the spinel linewidths of these three samples are significantly different. Even in the slow-oxidation mode, physical and chemical processes may depend delicately on the actual oxidation rate. These observations imply a considerable difference in the iron-oxide crystallite size for the A, B and C samples. Further, the iron-oxide layer is apparently

not continuous, but consists of very fine crystallites. A similar observation was made by Boggs *et al.*²³ in a microscopic study of the oxidation process for iron.

Although the lines for samples D and E are much sharper than for A, B and C, they, nevertheless, are still relatively broad. The average crystallite sizes for the oxide and the metallic iron were determined for all samples using the Scherrer relation (Table 1). The faint superlattice lines of samples D and E, observed in spite of the relatively small average crystallite size, seems to imply that some of the crystallites are large enough to have developed vacancy ordering.

To generalise, the X-ray studies imply that on slow oxidation of ultrafine aerosoled iron particles only partial oxidation occurs with the formation of finely divided oxide crystallites on the iron. On the other hand, on fast oxidation, all the iron is oxidised into crystallites that are relatively large.

Mössbauer studies

Mössbauer measurements were made on the five samples at 77 and 300 K; some spectra are shown in Figs 2, 3 and 4. To make an absorber, the powder was dispersed in acetone, dried in air, and pressed between two plates of Perspex or beryllium. The source was ⁵⁷Co in a chromium host. The spectrometer was conventional, and all but one of the spectra (Fig. 3*b*) were taken with a fly-back drive.

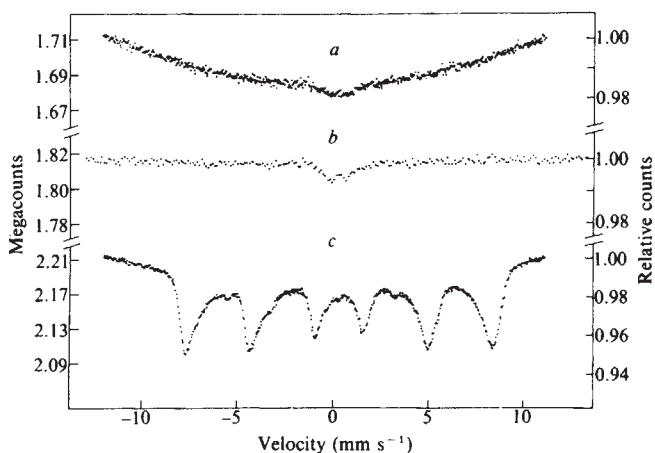


Fig. 3 Mössbauer spectra for aerosoled Fe particles subject to slow oxidation, sample B (238 Å). *a*, At 300 K; *b*, at 300 K, taken with a triangular waveform drive and folded; *c*, at 77 K.

Mössbauer spectra for samples A and B, both subjected to the slow-oxidation mode, are shown in Figs 2 and 3 respectively. An interesting and important feature is the lack of absorption at room temperature. Note that fine particles, close to or less than 100 Å in diameter but prepared by other methods, such as chemical precipitation, do display a central superparamagnetic absorption sometimes accompanied by hyperfine split patterns at $T = 300$ K. Therefore, the implication is that a majority of the ^{57}Fe nuclei in the aerosoled particles experience a recoil on absorption of the γ ray. Perhaps the iron atoms or ions are loosely bound within an aerosol particle, and further, any inter-particle interactions are relatively small. A weaker than normal binding would lead to a reduction in the Debye–Waller factor.

As the parabolic-shaped background introduces some ambiguity, a spectrum for sample B at 300 K was obtained with a triangular-shaped drive and a greater velocity range, and folded; it is shown as Fig. 3b. The small but non-zero central absorption shows that although the number of recoilless absorptions was

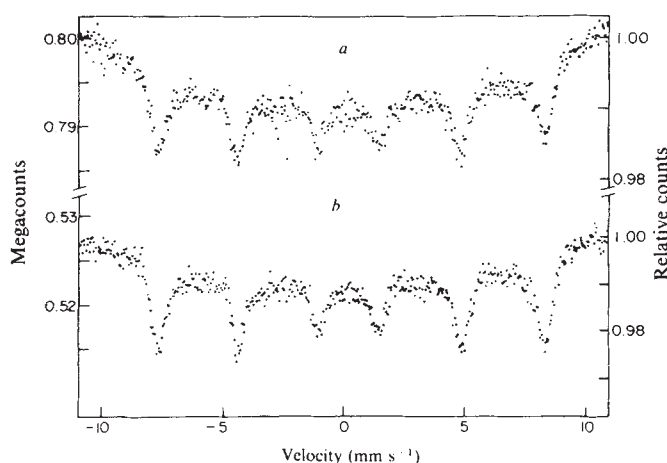


Fig. 4 Mössbauer spectra for aerosoled Fe particles subject to fast oxidation. *a*, Sample D (329 Å) at 300 K; *b*, sample E (366 Å) at 300 K.

small, the crystallites were in the superparamagnetic size range. This observation is fully compatible with the X-ray results.

In contrast, samples D and E, subjected to the fast-oxidation mode, exhibit hyperfine-split Mössbauer spectra at 300 K with, however, some reduction in the recoilless fraction as compared to bulk materials (Fig. 4*a, b*). When the temperature is elevated during the non-isothermal oxidation, not only do the oxide crystallites grow larger, but apparently the quality of crystallinity is also improved. Better developed crystallites would be expected to have strengthened atomic or ionic binding, and therefore a Debye temperature closer to that for the bulk.

In some situations, the Mössbauer effect can be used for phase analysis. By referring to standard spectra of α -Fe and the various iron oxides, the relative amounts of these phases can in principle be determined. By referring to Figs 2*b* and 3*c*, it is clear that both iron and iron-oxide phases are present. An earlier Mössbauer analysis of sample C established that the oxide is partially oxidised Fe_3O_4 , possibly a mixture of stoichiometric Fe_3O_4 and $\gamma\text{-Fe}_2\text{O}_3$ (ref. 10). A similar situation seems to apply for samples A and B. The oxidised fractions of samples, A, B and C were determined from the 77 K spectra by comparing the areas of the oxide and metallic iron patterns employing computer fitting and assuming equal recoilless fractions for the two phases (Table 1). For samples D and E, the Mössbauer spectra confirm the X-ray analysis that the particles are almost entirely $\gamma\text{-Fe}_2\text{O}_3$.

Table 2 Hyperfine field at 77 K for aerosoled iron particles subject to slow oxidation

Sample	Hyperfine field (kOe)			Linewidth (mm s ⁻¹)		
	Fe	Inner sextet	Outer sextet	Fe	Inner sextet	Outer sextet
A	243	470	507	0.400	0.994	0.645
B	347	465	503	0.493	1.179	0.673
C	344	451	494	0.492	1.285	0.773
Micrometre-sized $\gamma\text{-Fe}_2\text{O}_3$ *		508	525		0.562	0.533

One six-line pattern is assumed for metallic Fe and two six-line patterns are assumed for cubic iron-oxide.

* From ref. 25.

The hyperfine fields will now be discussed. In order to reduce the complexity of the analysis, the 77 K spectra of samples A, B and C were fitted with one six-line pattern for the iron and two six-line patterns for the iron oxides. This procedure is an oversimplification as the oxide is probably a mixture of $\gamma\text{-Fe}_2\text{O}_3$ and Fe_3O_4 in the Verwey state. The hyperfine fields and linewidths obtained are listed in Table 2. The iron hyperfine fields are close to the normal, bulk values, although the lines are somewhat broadened. However, the oxide's hyperfine fields are 30 to 50 kOe lower than those for micrometre-sized $\gamma\text{-Fe}_2\text{O}_3$ particles at 77 K. As a particle is made up of a central iron core covered with finely divided oxide crystallites, the magnetic moments of the oxide crystallites experience a considerable interaction at the iron interface. Then, the tendency towards superparamagnetic behaviour may be largely quenched at 77 K. However, fluctuations in the oxide's magnetisation direction may still be taking place, and if so, would lead to a reduction of the hyperfine field. This hypothesis is a modification of a collective magnetic excitation model proposed by Mørup and Topsøe²⁴. In other words, the diminished value of the hyperfine field is an intrinsic size effect complicated by the exchange interaction at the iron interface.

Thus the oxidation mode used with ultrafine aerosoled iron particles profoundly influences the morphology of the oxide scales and the recoilless (Mössbauer) fraction. Some magnetic properties of these particles can therefore be controlled by the conditions of oxidation, and this feature should be of great utility in small iron particle applications.

This research was supported by the Natural Sciences and Engineering Research Council of Canada.

Received 19 July; accepted 3 September 1979.

- Kimoto, K., Kamiya, Y., Nonoyama, M. & Uyeda, R. *Jap. J. appl. Phys.* **2**, 702–713 (1963).
- Gen, M. Y., Velichenkova, E. A., Eremina, I. V. & Ziskin, M. S. *Sov. Phys.-Solid State* **6**, 1274–1277 (1964).
- Tasaki, A., Tomiyama, S., Iida, S., Wada, N. & Uyeda, R. *Jap. J. appl. Phys.* **4**, 707–711 (1965).
- Davies, D. E., Evans, U. R. & Agar, J. N. *Proc. R. Soc.* **225A**, 443–462 (1954).
- Sewell, P. B. & Cohen, M. J. *Electrochem. Soc.* **111**, 501–508 (1964).
- Channing, D. A. & Graham, M. J. *Corrosion Sci.* **12**, 271–289 (1972).
- Goursat, A. G. & Smeltzer, W. W. *Oxidation of Metals* **6**, 101–116 (1973).
- van Diepen, A. M., Vledder, H. J. & Langereis, C. *Appl. Phys.* **15**, 163–166 (1977).
- Yatsuya, S., Hayashi, T., Akoh, H., Nakamura, E. & Tasaki, A. *Jap. J. appl. Phys.* **17**, 355–359 (1978).
- Haneda, K. & Morrish, A. H. *Surface Sci.* **77**, 584–590 (1978).
- Haneda, K. & Morrish, A. H. *J. Phys. (Paris)* **40**, C2–91–93 (1979).
- Marshall, S. W. & Wilenzick, R. M. *Phys. Rev. Lett.* **16**, 219–221 (1966).
- Roth, S. & Hörl, E. M. *Phys. Lett.* **25A**, 299–300 (1967).
- van Wieringen, J. S. *Phys. Lett.* **26A**, 370–371 (1968).
- MacRae, A. U. & Germer, L. H. *Phys. Rev. Lett.* **8**, 489–490 (1962).
- Viegers, M. P. A. & Trooster, J. M. *Phys. Rev. B* **15**, 72–83 (1977).
- von Eynatten, G. & Bömmel, H. E. *Appl. Phys.* **14**, 415–421 (1977).
- Matsushita, E. & Matsubara, T. *Prog. theor. Phys.* **59**, 15–22 (1978).
- Feitknecht, W. & Durtschi, A. *Helv. chim. Acta* **47**, 174–181 (1964).
- Tasaki, A., Takao, M. & Tokunaga, H. *Jap. J. appl. Phys.* **13**, 271–276 (1974).
- Haneda, K. & Morrish, A. H. *J. Phys. (Paris)* **38**, C1–321–323 (1977).
- Haneda, K. & Morrish, A. H. *Solid State Commun.* **22**, 779–782 (1977).
- Boggs, W. E., Kachik, R. H. & Pellissier, G. E. *J. electrochem. Soc.* **114**, 32–39 (1967).
- Mørup, S. & Topsøe, H. *Appl. Phys.* **11**, 63–66 (1976).
- Haneda, K. & Morrish, A. H. *Phys. Lett.* **64A**, 259–262 (1977).

A different genetic code in human mitochondria

B. G. Barrell, A. T. Bankier & J. Drouin*

MRC Laboratory of Molecular Biology, Hills Road, Cambridge, UK

Comparison of the human mitochondrial DNA sequence of the cytochrome oxidase subunit II gene and the sequence of the corresponding beef heart protein shows that UGA is used as a tryptophan codon and not as a termination codon and suggests that AUA may be a methionine and not an isoleucine codon. The cytochrome oxidase II gene is contiguous at its 5' end with a tRNA^{Asp} gene and there are only 25 bases at its 3' end before a tRNA^{Lys} gene. These tRNAs are different from all other known tRNA sequences.

THE genetic code has been considered to be universal since the early work on *Escherichia coli* and mutant eukaryotic proteins. Once the code was established it was argued that any change would be lethal. This view was substantiated by the development of rapid RNA and DNA sequencing methods which have explored a wide variety of gene sequences that could be related to their protein sequences. We present evidence here, however, that mitochondria have an altered genetic code. This conclusion is based on the nucleotide sequence of a region of human mitochondrial DNA which was shown to code for an amino acid sequence homologous to the known protein sequence of the cytochrome oxidase subunit II (COII) of bovine mitochondria¹. The homology was such that it was concluded that this region of the DNA was coding for the human COII gene. However, there were three TGA codons in the reading frame that was coding for the protein. This demonstrated that UGA was not acting as a termination codon. Moreover, the amino acid present in the bovine protein in all positions where TGA occurred in the human DNA sequence was tryptophan. Such a correspondence could only be satisfactorily explained if UGA was coding for tryptophan rather than for termination. Similar evidence is also presented that suggests that AUA is a methionine codon and not isoleucine.

Human mitochondria have a separate genetic system with a DNA genome of molecular weight 10×10^6 . Figure 1 shows the organisation of the human mitochondria genome^{2,3} aligned with the *Mbo*I restriction enzyme map. HeLa cell mitochondrial DNA (mtDNA) has been shown by hybridisation to code for a 12S and a 16S ribosomal RNA and at least 19 tRNAs²⁻⁴. HeLa cell mitochondrial translation products are less well defined and only cytochrome oxidase subunits I, II and III have been identified so far⁵. By analogy with other mitochondria systems (for review see ref. 6) genes for four proteins of the ATPase complex and one of the cytochrome *bc*₁ complex should also be present. However, it has become apparent recently that more proteins (at least 19) are coded for by HeLa cell mtDNA⁷. Both strands of HeLa cell mtDNA are completely transcribed symmetrically^{8,9}. The rRNAs, the majority of the rRNAs and all but one of the polyadenylated RNAs hybridise to the heavy strand (H strand)^{2,4,8,10}. Thus, the light strand (L strand) is defined as the main coding strand, having the same sequence as the rRNAs, tRNAs and mRNAs.

In the sequence of the COII gene region presented here we have identified two putative tRNA genes flanking the COII gene. A tRNA^{Asp} gene is 'butt-jointed' to the initiation codon of the COII gene, that is, there is no intergenic space between them, and there are only 25 nucleotides between the termina-

tion codon of the COII gene and a tRNA^{Lys} gene. These tRNA genes are unusual in that they differ considerably in the 'D loop' and 'T ψ C loop' from all other known tRNA sequences.

DNA sequence analysis

*Mbo*I restriction enzyme fragments of human mtDNA obtained from a single term placenta have been cloned in the *Bam*HI site of pBR322 (ref. 42). Sequence analysis of clones pmt 110, 140 and 101, containing *Mbo*I fragments 6a, 15 and 6b, respectively (see Fig. 1), was by the chain termination method of Sanger *et al.*¹¹. Single-stranded template DNA was prepared by the exonuclease III method of Smith¹². By cleaving the duplex circular DNA at either the unique pBR322 *Hind*III site or the unique pBR322 *Sal*I site and digesting with exonuclease III, either strand of the region containing the inserted DNA was obtained pure for the primed synthesis DNA sequencing reaction. Small restriction fragment primers were prepared both from the pBR322 sequences flanking the insert, so as to prime into the insert from either side, and from within the insert.

The sequence determined is shown in Fig. 2. Sequence analysis of the *Alu*I restriction fragment spanning *Mbo*I fragment 15 which was cloned separately shows that there are no small *Mbo*I fragments between *Mbo*I fragments 6a, 15 and 6b (A. R. Coulson, personal communication). Two examples of chain termination sequencing gels are shown in Fig. 3. Figure 3a shows the sequence from -120 through the tRNA^{Asp} gene and

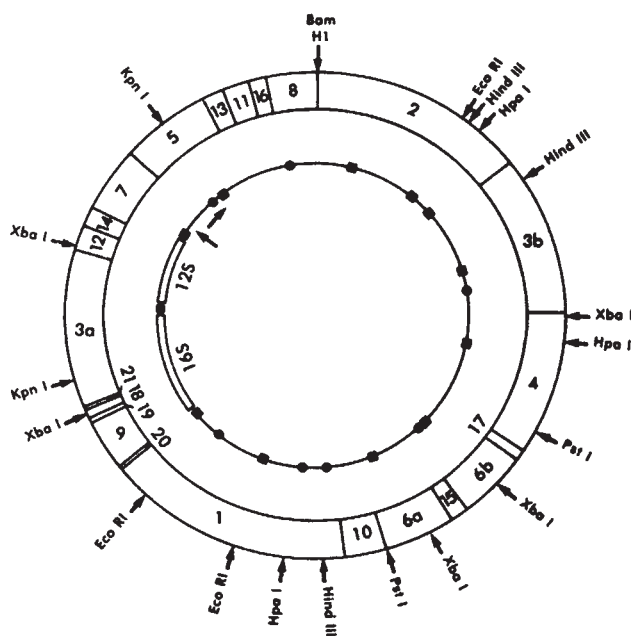


Fig. 1 The genetic map of the human mtDNA genome^{2,3} is aligned with the *Mbo*I restriction enzyme map⁴². The precise order of fragments 21, 18 and 19 is not known. The sites of cleavage of some other enzymes are also shown^{43,44}. The origin and direction of H-strand synthesis is shown^{43,44}. The L-strand sequence 5' to 3' is anticlockwise and codes for the 12S and 16S rRNAs and tRNAs marked ■ (complementary to H strand). The H strand codes for the tRNAs marked ● (complementary to L strand). The COII gene is centred approximately on *Mbo*I fragment 15.

* Present address: Department of Biochemistry and Biophysics, University of California, San Francisco, California 94143.

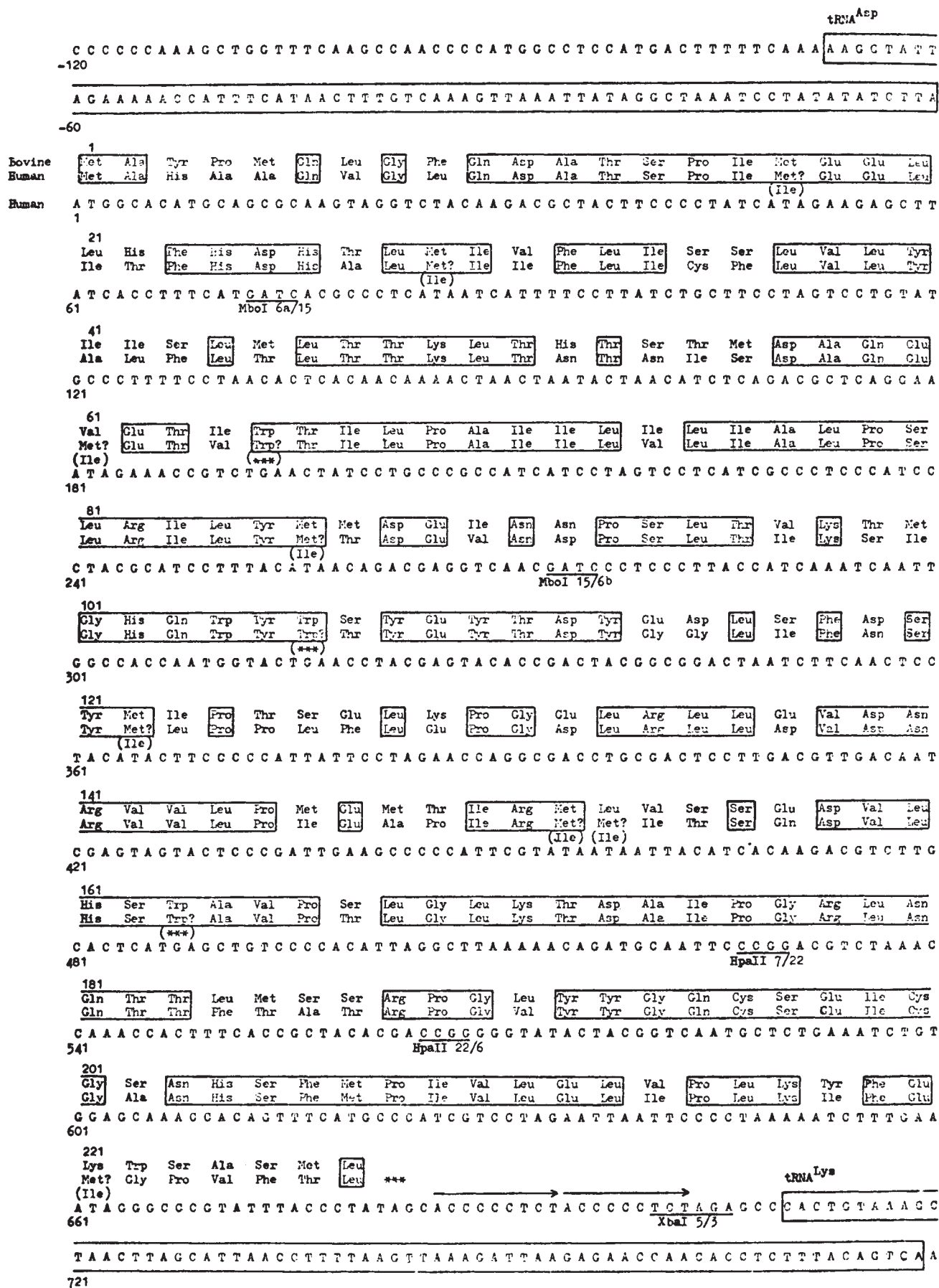


Fig. 2 The sequence of the COII gene region showing the position of the two tRNA genes and the COII DNA sequence aligned with the bovine COII protein sequence¹. The predicted human protein sequence is compared with the bovine sequence and homologous amino acids are shown boxed using the codons AUA as methionine and UGA as tryptophan. Their normal assignments isoleucine and termination (denoted by ***) are shown underneath. The sequence can be aligned with the genetic and restriction maps shown in Fig. 1 by the restriction enzyme sites MboI and XbaI shown. A 9-base repeat at the end of the COII gene is also shown.

the beginning of the COII gene to the *Mbo*I site at position +73, and Fig. 3b shows the sequence obtained using *Hpa*II fragment 22 as a primer from position +521 to the *Mbo*I site at position +274. The positions of the TGA and ATA codons in these regions are shown.

tRNA genes

Three tRNA genes have been mapped in this region of the genome², two hybridising to the H strand and one to the L strand (see Fig. 1). In the sequence presented in Fig. 2 we have only been able to locate two tRNA genes, both of which are coded on the L strand, that is, the tRNA products would hybridise to the H strand. The locations of these tRNAs agree well with the hybridisation map positions² shown in Fig. 1, and from their positions in the sequence they probably correspond to H5 and H6 according to the nomenclature of Angerer *et al.*². However, if this assignment is correct there should be a tRNA gene close to the tRNA^{Lys} gene on the opposite strand that we have been unable to find. The tRNA genes were located by searching for base-paired cloverleaf structures using the computer programs HAIRPN¹³ and TRNA (R. Staden, unpublished).

The sequences of the two putative tRNA genes are shown in the cloverleaf form in Fig. 4. If these tRNAs have CCA at their 3' ends then this is not encoded in the DNA. The sequences in the D loop (left-hand loop) and the T ψ C loop (right-hand loop) of both tRNA genes differ considerably from the corresponding sequences found in all other tRNAs (see collection of 209 tRNA sequences compiled by Sprinzl *et al.*¹⁴). In the tertiary structure of yeast tRNA^{Phe} (refs 15, 16) these two loops are hydrogen bonded together by conserved nucleotides not found in the two mitochondrial tRNA sequences. An examination of the primary structures of the two genes in these regions has not yet revealed how their respective D and T ψ C loops interact in the manner of yeast tRNA^{Phe}. A more detailed discussion of these and other human mitochondrial tRNA genes will be published separately.

UGA and UGG are both tryptophan codons in human mtDNA

The most interesting aspect of the sequence is in the part coding for the COII gene which is identified by the high homology with the bovine protein sequence¹. When the human DNA sequence is aligned with the beef protein sequence as shown in Fig. 2, it becomes apparent that there are three 'in phase' UGA (*opal*) termination codons within the gene. The possibility that these are present in intervening sequences can be excluded by several criteria. First, the gene seems to be the exact length needed to code for its product, without interruption, from the AUG initiation codon to the UAG (*amber*) termination codon. Second, the UGA codons are in regions of very high homology between the beef and predicted human protein sequences. Finally, and most important, is the fact that they all align with tryptophans in the bovine protein. This suggests very strongly that UGA is a tryptophan codon in this genetic system and not a termination codon. There are five tryptophan residues in the bovine COII sequence, three of them opposite UGA codons, one opposite a UGG tryptophan codon and one opposite a GGG glycine codon. The latter is in a region where there is no homology with the bovine protein sequence at position 664 in the DNA sequence shown in Fig. 2. Tryptophan is normally coded for by a single codon, UGG, which is translated by a tRNA^{Trp} with a CCA anticodon in both prokaryotes¹⁷ and eukaryotes^{18,19}. However, there is a precedent for UGA being used as a tryptophan codon. tRNA^{Trp} from an *su*⁺ UGA strain of *E. coli* (CAJ64) suppresses a UGA mutation in lysozyme mRNA during cell-free protein synthesis and synthesises poly-tryptophan from a repeating UGA polymer^{20,21}. However, in both assays there was a low synthesis of product using tRNA^{Trp} from the *su*⁻ *E. coli* CA244. This, coupled with the observation that *in vivo* UGA codons are leaky in *su*⁻ strains^{22,23}, suggested that the low level of UGA suppression in *su*⁻ strains was caused by the normal tRNA^{Trp}. Also the low level of readthrough of the

Q β coat protein UGA termination codon in *su* hosts was shown to occur by insertion of tryptophan and a functional longer protein necessary for infectivity was found in the phage particle^{24,25}. Thus, there is a precedent in prokaryotes that UGA can be used as a tryptophan codon, albeit infrequently.

The codons UGA and UGG are adjacent in the genetic code (see Fig. 5) and could thus be recognised specifically by a tRNA^{Trp} having the anticodon UCA according to the 'wobble hypothesis' (ref. 26) where U in the first position of the anticodon could pair with A or G in the third position of the codon. However, tRNA^{Trp} from both the *su*⁻ and *su*⁺ UGA *E. coli* strains have CCA as their anticodons and the suppressor tRNA^{Trp} has a G24 $\rightarrow$ A24 in the semi-invariant base pair in the 'D arm' (ref. 17). This must somehow alter the tertiary structure of the suppressor tRNA to allow the C in the first position of the anticodon to pair with the A in the third position of the UGA codon. Although neither the human mitochondrial tRNA^{Trp} nor its gene has yet been characterised there is evidence from charging experiments⁴ of unfractionated mitochondrial tRNA for a mitochondrially coded tRNA^{Trp}.

It thus seems clear that if this gene is expressed in its entirety, UGA and UGG are both used as tryptophan codons in the genetic code of human mitochondrial DNA. The sequence of the yeast mitochondrial COII gene also has UGA codons opposite tryptophan residues when it is aligned with the bovine COII protein sequence^{27,41}. The use of UGA as a tryptophan codon would preclude the use of the cytoplasmic termination factor which corresponds to all three termination codons²⁸. Prokaryotes use two factors, R1, which corresponds to UAA and UAG, and R2, which corresponds to UAA and UGA²⁹. Thus, it is likely that the mitochondria has a factor analogous to R1.

Does AUA code for methionine in human mtDNA?

There are two codons in the genetic code that are each the sole codon for a single amino acid. The case of UGG for tryptophan has been discussed above. The other codon is AUG, which codes for methionine, and in the same box isoleucine is encoded by AUC, AUU and AUA. All other boxes can be read using G-U wobble²⁵ by one tRNA that is specific for codons ending in C and U and another that is specific for codons ending in A and G. The main exception to this is when the anticodon contains modified bases that can restrict the coding properties. Thus, with the UGA/tryptophan precedent in mind, can AUA code for methionine? There are 15 internal methionine residues in the beef COII sequence and only one of these is aligned with an AUG codon but five of them are aligned with AUA codons (Fig. 2). There are eight AUA codons, five aligned with methionine, one with valine, one with leucine and one with lysine. None is aligned with isoleucine codons. Thus, there are two possibilities: either by coincidence the bovine methionine residues in these positions are being preferentially replaced by isoleucines which are all coded for by AUA, or there is another change in the code and AUA is being recognised as a methionine codon. AUA and AUG could both be recognised by a tRNA having the anticodon UAU according to the wobble hypothesis²⁶.

In view of the UGA/UGG precedent we think that the above data suggest that AUA and AUG are methionine codons. However, isoleucine and methionine are both hydrophobic amino acids and confirmation will depend on the determination of the human COII protein sequence.

If it is assumed that AUA is a methionine codon and UGA a tryptophan codon, the bovine protein and the predicted human protein sequences are 72% identical. The conserved amino acids are shown boxed in Fig. 2. This leaves 62 out of 227 amino acids in bovine COII that are different in the human COII. It is striking that 22 of these differences involve either methionine or serine aligning with other amino acids, eight of them threonine, using the codons ACA and ACC. However, both of these codons also align with threonine, and with the data shown in

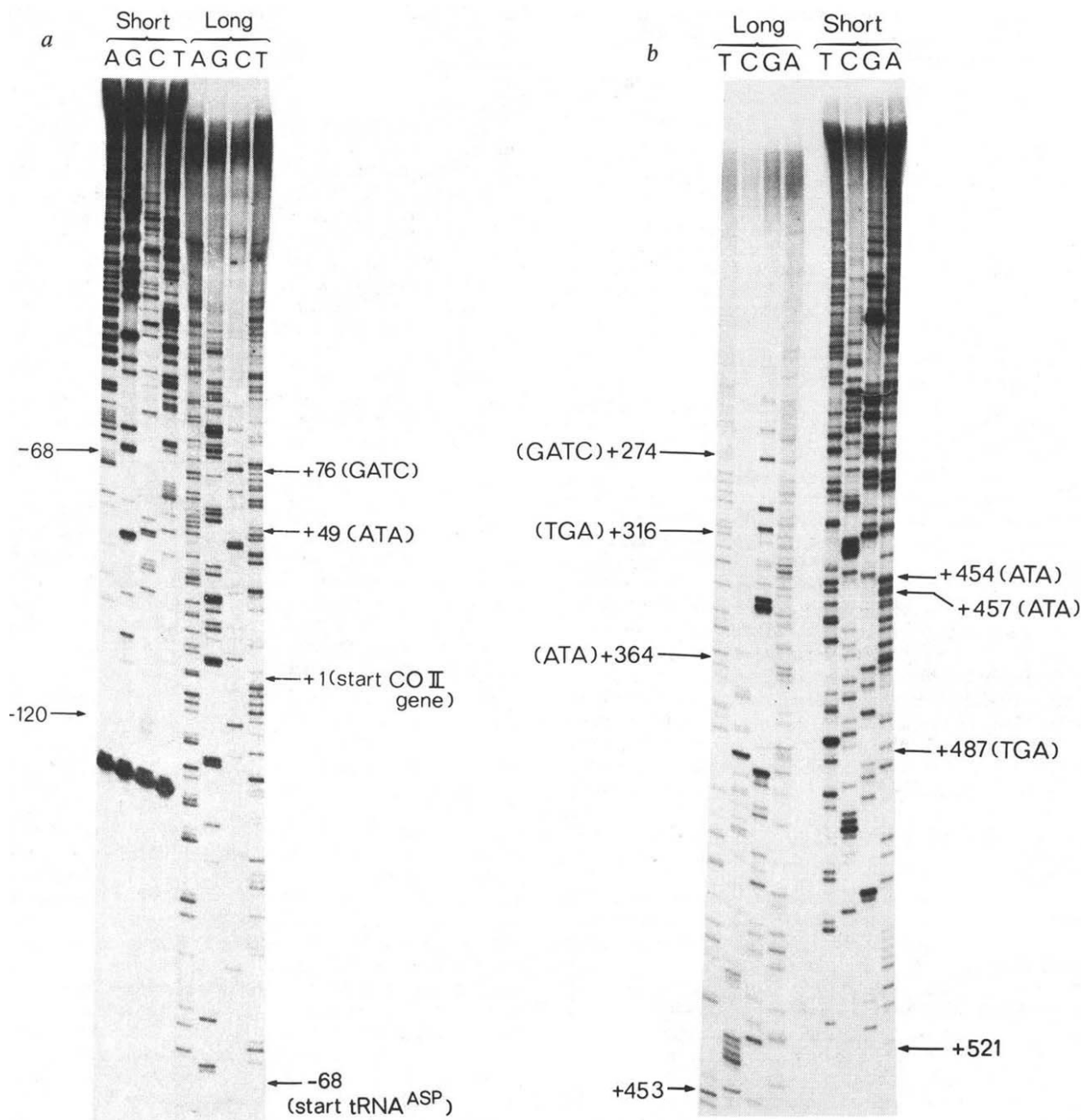


Fig. 3 Two examples of chain termination sequencing gels in the COII gene region. *a* Shows the use of a small restriction fragment primer in *Mbo*I fragment 6a primed on 'H-strand' template prepared from clone pmt 110 (see text) by the exonuclease III method of Smith¹². The sequence corresponding to that given in Fig. 2 can be read from base -120 to the *Mbo*I site at +76 which is the junction between the clone of *Mbo*I 6a and pBR322. The starts of the tRNA^{ASP} gene and the COII gene are shown along with the ATA codon at position +49. A short run and a long run of the sequencing reactions on the same 8% polyacrylamide thin gel⁴⁶ are shown. *b* Shows a similar experiment using the fragment *Hpa*II 22 as a primer on 'L-strand' template prepared from clone pmt 110 (*Mbo*I fragment 6b, see text). For ease of reading the track order A, G, C, T has been changed to the complementary order T, C, G, A so that the gel can be read as the L-strand sequence 5' to 3', from top to bottom. The sequence from the junction between pBR322 and *Mbo*I 6b at position +274 can be read to position +521. The positions of the UGA and AUA codons are shown.

Fig. 2 there is no clear indication of other coding changes. The one difference between the yeast mitochondrial ATPase subunit 9 protein sequence³⁰ and the sequence of its gene³¹ is a threonine aligned with a CUA codon. In the human COII gene, 11 out of 12 CUA codons align with leucine so that this cannot be a coding change in human mtDNA. However, it is possible that other coding changes will be found in mtDNA and there may be different codes in the mitochondria of different species.

Codon usage in the COII gene

Figure 5 shows the suggested code in human mitochondria with AUA as possibly methionine and UGA as tryptophan. The

number of times each codon appears in the COII gene is also shown. All amino acids are used and nearly all codons. Only one of the serine AGU/C set is used and none of the arginine AGA/G set. Excluding the UAG termination codon, only 16 out of 227 codons end in G. This reflects the low G content found in the L strand generally (unpublished results). Specifically in this region the composition is A, 29.9%; C, 30.2%; T, 25.8% and G, 14.1%. The low G content may be of significance when considering the evolution and use of the coding changes proposed here. Including AUA as methionine and UGA as tryptophan the ratio of codons ending in A to those ending in G is 5:1.

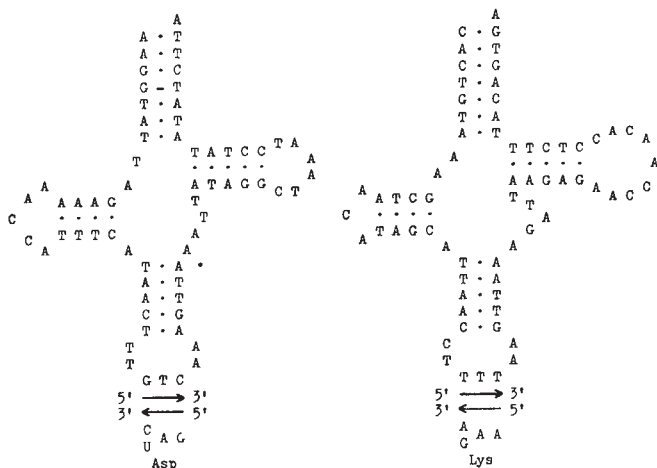


Fig. 4 The DNA sequences of the $tRNA^{Asp}$ and $rRNA^{Lys}$ genes are shown arranged in the cloverleaf conformation. The CCA sequence found at the 3' end of all tRNAs is not encoded in the DNA sequence. The presumed codons that these tRNAs would recognise by G-U wobble²⁶ are indicated.

It is also interesting to consider the codon usage in relation to the number of tRNAs found to be encoded by human mtDNA. The highest number of tRNAs so far found to be coded by mammalian mtDNA is 21 (ref. 32) out of the minimum number required using G-U wobble of 32. If the AUA coding change is substantiated then a minimum of 31 would be required. On the basis of the relatively small sample of codons of the COII gene, it is probably reasonable to assume that in the whole genome all codons are used, although some may be used rarely. There is no evidence in mammalian mitochondria to suggest that any RNA is imported, and so there may be a complete set of mitochondrially coded tRNAs. Otherwise, it is difficult to see how 21 tRNAs could recognise all codons without some degree of misreading. However, it is possible that the smaller rRNAs, the novel features of the tRNAs, the possible coding changes discussed here and a limited set of tRNAs might indicate that a different protein synthesis decoding mechanism operates in the mitochondria. Selective use of a 'two out of three mechanism' (refs 33, 34) would only require 23 or 24 tRNAs, depending on the coding changes.

Organisation of genes in the COII region

Attardi *et al.*⁷ discussed two models for the organisation of the tRNA genes with respect to the protein coding sequences. As can be seen in Fig. 1 the tRNA genes are scattered more or less uniformly around the genome and on both strands. These genes could either separate the sequences coding for the mRNA (the punctuation model) or could reside in them in the manner of intervening sequences (the insert model). The COII gene is flanked by two tRNA genes as shown in Fig. 2 but surprisingly, the $tRNA^{Asp}$ gene is actually contiguous with the COII gene, with no noncoding nucleotides in between. Thus, it is possible that if there are sequences involved in ribosome recognition preceding the initiation codon these lie in the $tRNA^{Asp}$ gene. No sequence corresponding to the *E. coli* ribosome recognition site is found^{35,36}. There is a sequence similar to that postulated to have the same function in eukaryotes³⁷ but there is no evidence that this interaction occurs in eukaryotes and in any case mitochondria have their own rRNAs, which are much smaller than both their prokaryote and eukaryote counterparts. The possibility of a leader peptide which is subsequently processed is ruled out by in-phase UAA termination codons preceding the initiation codon.

The contiguous nature of the two genes raises the obvious difficulty in processing the primary transcript. Both strands of the mtDNA have been shown to be completely transcribed and it is not known whether there are additional promoters. If a full length transcript of the H strand is processed to give the rRNAs, and the tRNAs and mRNAs, the latter being polyadenylated at

some stage, then a single cleavage between the two genes would leave no 5'-leader sequence on the COII gene mRNA. Therefore, if initiation of translation of the COII mRNA required signals in the sequence preceding the initiation codon, the tRNA would either have to be released after the cessation of translation of the mRNA or have to be transcribed separately. An intriguing possibility is that the tRNA could be spliced out of the transcript in the manner of an intervening sequence, although this seems unlikely; no evidence has yet been found for intervening sequences in human mtDNA.

There is a short noncoding region (25 bases) between the end of the COII gene and the $tRNA^{Lys}$ gene and this contains a 9-base repeat, as shown in Fig. 2. The sequence AAUAAA is presumed to be involved in polyadenylation of eukaryotic mRNAs and the nearest is 224 bases downstream of the 3' end of the COII gene (unpublished results). If this is the signal for polyadenylation of the COII mRNA, a similar problem to that of the $tRNA^{Asp}$ regarding the processing of the $tRNA^{Lys}$ arises.

There has been considerable speculation that mitochondria have evolved from bacteria that had entered into a symbiotic relationship with their host (for review see ref. 6). The economical use of the coding capacity of the DNA is more characteristic of prokaryotes, in particular bacteriophage DNAs such as ΦX (ref. 38), but the eukaryotic viruses such as SV40 (refs 39, 40) show similar economy. Thus, it is difficult to draw any conclusions as to whether this genetic system is more similar to prokaryotes or eukaryotes on this basis. If the endosymbiotic theory is correct, the different genetic code may represent a 'frozen', more primitive code, for it is unlikely that once mitochondria became essential to their 'host' the code would be able to change. Whatever their origins the novel features of the mitochondria discussed here seem to require that they be considered a separate class from the prokaryotic and eukaryotic genetic systems.

Since this paper was submitted, Macino *et al.*⁴¹ have also demonstrated the use of UGA as tryptophan in the yeast mtDNA COII gene. Also, recent work by F. Sanger and A. R. Coulson (personal communication) has identified the sequence coding for the tryptophan tRNA gene in human mtDNA. As predicted, this structure has the anticodon UCA which would pair with UGA and UGG using G-U wobble.

We thank Dr G. Buse for communicating to us the bovine COII protein sequence before publication, and Drs F. Sanger and J. E. Walker for advice and helpful discussions.

		Second letter											
		U			C			A			G		
First letter	U	UUU } Phe 3	UUC } 7	UUA } 4	UUG } 1	UCU } 1	UCC } 4	UCA } 4	UCG } 0	UAU } 1	UAC } 8	UAA } 0	UAG } 1*
										UGU } 1	UGC } 2	UGA } 3	UGG } 1
C	CUU } 7	CUC } 6	CUA } 12	CUG } 3	CCU } 1	CCC } 9	CCA } 3	CCG } 2	CAU } 2	CAC } 4	CAA } 6	CAG } 1	
										CGU } 2	CGC } 1	CGA } 3	CGG } 0
A	AUU } 7	AUC } 15	AUA } 8	AUG } 2	ACU } 5	ACC } 8	ACA } 8	ACG } 0	AAU } 2	AAC } 5	AAA } 4	AAG } 0	
										AGU } 1	AGC } 0	AGA } 0	AGG } 0
G	GUU } 1	GUC } 7	GUA } 5	GUG } 0	GCU } 4	GCC } 5	GCA } 4	GCG } 1	GAU } 3	GAC } 8	GAA } 8	GAG } 3	
										GGU } 2	GGC } 4	GGA } 3	GGG } 2

Fig. 5 The code in human mtDNA suggested by the results presented here is shown along with the number of times each codon is used in the COII gene. AUA and UGA are normally isoleucine and termination, respectively.

Received 24 July; accepted 28 September 1979.

1. Steffens, G. J. & Buse, G. *Hoppe-Seyler's Z. physiol. Chem.* **360**, 613 (1979).
2. Angerer, L., Davidson, N., Murphy, W., Lynch, D. C. & Attardi, G. *Cell* **9**, 81 (1976).
3. Ojala, D. & Attardi, G. *Plasmid* **1**, 78 (1977).
4. Lynch, D. C. & Attardi, G. *J. molec. Biol.* **102**, 125 (1976).
5. Hare, J., Ching, E. & Attardi, G. (in preparation).
6. Borst, P. *Trends biochem. Sci.* **2**, 31 (1977).
7. Attardi, G. et al. *Proc. ICN-UCLA Meet. Extrachromosomal DNA*, March 1979 (in the press).
8. Aloni, Y. & Attardi, G. *Proc. natn. Acad. Sci. U.S.A.* **68**, 1957 (1971).
9. Murphy, W., Attardi, B., Tu, C. & Attardi, G. *J. molec. Biol.* **99**, 809 (1975).
10. Almaric, F., Merkel, C., Gelfand, R. & Attardi, G. *J. molec. Biol.* **118**, 1 (1978).
11. Sanger, F., Nicklen, S. & Coulson, A. R. *Proc. natn. Acad. Sci. U.S.A.* **74**, 5463 (1977).
12. Smith, A. J. H. *Nucleic Acids Res.* **6**, 831 (1979).
13. Staden, R. *Nucleic Acids Res.* **5**, 1013 (1978).
14. Sprinzl, M., Grütter, F. & Gauss, D. H. *Nucleic Acids Res. Spec. Suppl.*, r15 (1979).
15. Ladner, J. E. et al. *Proc. natn. Acad. Sci. U.S.A.* **72**, 4414 (1975).
16. Kim, S. H. et al. *Science* **185**, 435 (1974).
17. Hirsh, D. *J. molec. Biol.* **58**, 439 (1971).
18. Keith, G., Roy, A., Ebel, J. P. & Dirheimer, G. *Biochimie* **54**, 1404 (1972).
19. Harada, F., Sawyer, R. C. & Dahlberg, J. E. *J. biol. Chem.* **250**, 3487 (1975).
20. Chan, T. S. & Green, A. *J. molec. Biol.* **49**, 231 (1970).
21. Hirsh, D. & Gold, L. *J. molec. Biol.* **58**, 459 (1971).
22. Katz, E. thesis, Cambridge Univ. (1969).
23. Roth, J. R. *J. Bact.* **102**, 467 (1970).
24. Wiener, A. M. & Weber, K. *Nature new Biol.* **234**, 206 (1971).
25. Wiener, A. M. & Weber, K. *J. molec. Biol.* **80**, 837 (1973).
26. Crick, F. H. C. *J. molec. Biol.* **19**, 548 (1966).
27. Fox, T. D. *Proc. natn. Acad. Sci. U.S.A.* (in the press).
28. Beaudet, A. L. & Caskey, C. T. *Proc. natn. Acad. Sci. U.S.A.* **68**, 619 (1971).
29. Scolnick, E., Tompkins, R., Caskey, T. & Nirenberg, M. *Proc. natn. Acad. Sci. U.S.A.* **61**, 768 (1968).
30. Sebald, W. & Wachter, E. in *29th Mosbacher Colloqu. Energy Conservation in Biological Membranes* (eds Schafer, G. & Klingenberg, M. 228, (Springer, Berlin, 1978).
31. Hensgens, L. A. M., Grivell, L. A., Borst, P. & Bos, J. L. *Proc. natn. Acad. Sci. U.S.A.* **76**, 1663 (1979).
32. Aujame, L. & Freeman, K. B. *Nucleic Acids Res.* **6**, 455 (1979).
33. Mitra, S. K., Lustig, F., Åkesson, B., Lagerkvist, U. & Strid, L. *J. biol. Chem.* **252**, 471 (1977).
34. Lagerkvist, U. *Proc. natn. Acad. Sci. U.S.A.* **75**, 1759 (1978).
35. Shine, J. & Dalgarno, L. *Eur. J. Biochem.* **57**, 221 (1975).
36. Steitz, J. A. & Jakes, K. *Proc. natn. Acad. Sci. U.S.A.* **72**, 4734 (1975).
37. Hagenbuchle, O., Santer, M. & Steitz, J. A. *Cell* **13**, 551 (1978).
38. Sanger, F. et al. *Nature* **265**, 687 (1977).
39. Fiers, W. et al. *Nature* **273**, 113 (1978).
40. Reddy, V. B. et al. *Science* **200**, 494 (1978).
41. Macino, G., Coruzzi, G., Nobrega, F. G., Li, M. & Tzagoloff, A. *Proc. natn. Acad. Sci. U.S.A.* **76**, 3784 (1979).
42. Drouin, J. *J. molec. Biol.* (submitted).
43. Brown, W. M. & Vinograd, J. *Proc. natn. Acad. Sci. U.S.A.* **71**, 4617 (1974).
44. Robberson, D. L., Clayton, D. A. & Morrow, J. F. *Proc. natn. Acad. Sci. U.S.A.* **71**, 4447 (1974).
45. Crews, S., Ojala, D., Posakany, J., Nishiguchi, J. & Attardi, G. *Nature* **277**, 192 (1979).
46. Sanger, F. & Coulson, A. R. *FEBS Lett.* **87**, 107 (1978).

letters

Where can antimatter be hidden in the Universe?

Yu. A. Beletsky, A. I. Bugrij, E. S. Martynov
& A. A. Trushevsky

Institute for Theoretical Physics, Academy of Sciences of the Ukrainian SSR, Kiev 130, USSR

Undoubtedly complete symmetry of charge in the initial state of the Universe is an attractive idea. However, analysis of observational data¹ indicates that the visible Universe contains mostly particles of positive baryon number. Attempts²⁻⁶ to reconcile the assumption of initial symmetry with this observed asymmetry have met with some difficulties. However, if one accepts that the Universe is symmetric in baryon charge, then there must be regions of space or objects which contain at least as much antimatter as the matter which we observe. We propose here that the hypothesis of primordial black holes (PBHs)^{7,8} offers a simple and economic solution of the problem. Because of the well-known 'no hair' theorems the baryonic charge of PBHs cannot be observed, and hence PBHs are ideal stores for antimatter.

Extra antibaryons can be captured by PBHs either because of fluctuations in the density of the baryonic charge⁹ or for dynamic reasons. Here we concentrate on the first possibility: we assume that in the early Universe the PBH happened to collect excess antibaryons. Then, after baryon-antibaryon annihilation we arrive at the present charge asymmetry.

To obtain some quantitative estimates we assume that in the hadronic era M black holes were created each containing N_i^+ baryons and N_i^- antibaryons and that their distribution in the i th PBH ($i = 1, 2, \dots, M$) is the gaussian

$$W(N_i^+) = (2\pi\Delta N_i^2)^{-1/2} \exp\{-(N_i^+ - \bar{N}_i)^2/2\Delta N_i^2\} \quad (1)$$

The mean number of particles $\bar{N}_i$ and the fluctuations ΔN_i^2 are taken to be equal for particles and antiparticles because of the charge symmetry of the strong interaction. The probability that the PBH contains N_u extra antibaryons is

$$\begin{aligned} W(N_u) &= \int_0^\infty \left\{ \prod_{i=1}^M \frac{dN_i^+ dN_i^-}{2\pi\Delta N_i^2} \exp\left[-\frac{(N_i^+ - \bar{N}_i)^2 + (N_i^- - \bar{N}_i)^2}{2\Delta N_i^2}\right] \right\} \\ &\times \delta\left[\sum_{i=1}^M (N_i^- - N_i^+) - N_u\right] \\ &= \left(4\pi \sum_{i=1}^M \Delta N_i^2\right)^{-1/2} \exp\left(-\frac{N_u^2}{4\sum_{i=1}^M \Delta N_i^2}\right) \end{aligned} \quad (2)$$

Equation (2) shows that the most favourable situation corresponds to a minimum (mean) asymmetry of black holes: the greater the mass contained in a PBH (the more it increases $\sum_{i=1}^M \Delta N_i^2$), the larger is the deviation.

Let us now estimate the maximum energy density (averaged over the whole of space) of unobservable forms of matter assuming the present value of the Hubble constant H and that the age of the Universe ($\sim 2 \times 10^{10}$ Myr) exceeds the age of the Earth ($\sim 5 \times 10^9$ Myr). This gives

$$Ht \leq f(\Omega)$$

where $\Omega = \rho/\rho_c$ is the ratio of the energy density of the whole matter to the critical density, and $f(\Omega)$ for the closed Universe has the form

$$f(\Omega) = \frac{\Omega}{(\Omega-1)^{3/2}} \left[\arcsin\left(\frac{\Omega-1}{\Omega}\right)^{1/2} - \left(\frac{\Omega-1}{\Omega}\right)^{1/2} \right]$$

It follows that

$$\Omega \leq 62.5$$

As the density of observable forms of matter $\rho \approx 0.03\rho_c$, then the ratio of the energy density of unobservable to observable forms of matter can reach 2×10^3 and, consequently, the mean asymmetry in PBH is $\sim 5 \times 10^{-4}$.

If matter in its early stages can be considered as an ideal gas, then $\Delta N_i \sim N_i$ and the probability $W(N_u)$ for N_u baryons in the Universe will be

$$W(N_u) \sim \exp \left\{ -\frac{N_u^2}{N} \right\} = \exp \{-\sigma N_u\}$$

where σ is a measure of the asymmetry in PBHs. As should have been expected, an asymmetric creation of PBHs is highly unlikely. Nevertheless 'the dice were cast only once', which gives us the opportunity to analyse the evolution of the Universe.

Note that the possibility for an asymmetric creation of PBHs can be considerably increased if matter at the early stage satisfies a non-ideal equation of state. For example, for van der Waals equation the free energy has the form¹⁰

$$F = -NT \ln \frac{e^{Vn_0(T)}}{N} - NT \ln \left(1 - \frac{Nb}{V} \right) + a^2 \frac{N^2}{V}$$

and

$$\overline{\Delta N^2} = T \left(\frac{\partial N}{\partial \mu} \right)_{v,T} = T \left(\frac{\partial^2 F}{\partial N^2} \right)^{-1}_{v,T} = \left[\frac{V^2}{N(V-Nb)^2} - \frac{2a}{TV} \right]^{-1}$$

Hence in the vicinity of a phase transition, $\overline{\Delta N^2}$ may become arbitrarily large and make the capture of extra antibaryons in PBHs probable. A van der Waals system of ultrarelativistic particles has been considered in detail elsewhere¹¹.

Note also, that this probability makes sense either when an ensemble of systems is indicated or when the event is repeated in time. Therefore, for the Universe as a whole it should be used with care. Of course, one can assume (without any hope of confirmation) that there are many universes which like ours originated in a big bang; we then live in 'the best of all worlds': in the world in which a fraction of the antimatter has been hidden in PBHs. Another possibility concerns an oscillating Universe, in which expansions are followed by collapses. In this case we should have to wait for the situation described above to be realised (with the formation of asymmetric PBHs).

The account of the evaporation of black holes given by Hawking¹² does not essentially change the situation; it only imposes limitations on the mass spectrum of PBHs¹³. Moreover, as the evaporation of black holes is a charge-symmetric process, the extra baryonic charge captured by PBHs will not be observable, even if the evaporation ceased and created a naked singularity, the maximon¹⁴.

Received 22 February; accepted 31 August 1979.

- Steigman, G. A. *Rev. Astr. Astrophys.* **14**, 339–372 (1976).
- Alfen, H. *Rev. mod. Phys.* **37**, 652–665 (1965).
- Omnes, R. *Phys. Rep.* **3C**, No. 1 (1972).
- Fomin, P. I. *Dok. Akad. Sci. Ukr. SSR*, **A12**, 831–834 (1975).
- Cline, D., McIntyre, P. & Rubbis, C. *Phys. Lett.* **66B**, 429–431 (1977).
- Sato, K. *Prog. theor. Phys.* **58**, 385–386 (1977).
- Zeldovich, Ya. B. & Novikov, I. D. *Astr. Zh.* **43**, 758–765 (1966).
- Hawking, S. W. *Mon. Not. R. astr. Soc.* **152**, 75–83 (1971).
- Harrison, E. R., *Phys. Rev.* **167**, 1170–1175 (1968).
- Landau, L. D. & Lifshitz, E. M. *Statistical Physics* (Pergamon, New York, 1958).
- Bugrij, A. I. & Trushevsky, A. A. Preprint ITP-78-82E, Kiev (1978).
- Hawking, S. W. *Commun. math. Phys.* **43**, 199–218 (1975).
- Frolov, V. P. *Usp. Fiz. Nauk* **118**, 473–504 (1976).
- Frolov, V. P. in *Einsteinovskiy Zbornik 1975* (Nauka, Moscow, 1978).

Structure of the uranian upper atmosphere

J. Churms*, J. L. Elliot† & E. Dunham†

* South African Astronomical Observatory, C.P., Republic of South Africa

† Department of Earth and Planetary Sciences, and Department of Physics, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Although the occultations of relatively bright stars by planets are rare events, they provide an important ground-based method for determining temperature, pressure and number density profiles of planetary upper atmospheres¹. The technique is particularly valuable for planets in the outer Solar System, whose atmospheres have not yet been probed by spacecraft missions. Since the atmosphere of Uranus had not yet been investigated by the occultation technique, we have observed and report here the occultation of the star SAO158687 by Uranus on 10 March 1977 (refs 2, 3).

A photometer was set up on the 0.46-m reflector at the Cape Observatory, South Africa that used an RCA photomultiplier with a gallium arsenide photocathode, and a 3-mm thick Schott RGN9 filter. The data were recorded on one channel of a chart recorder, while radio time signals were recorded on another channel. The time constant of the data recording system was ~ 3 s and the signal from the star produced a deflection of 1.0 cm on the chart. The chart was measured at intervals of 0.5 s.

The light curves were analysed using the inversion method of French, Elliot and Gierasch⁴. This procedure gives the number density, pressure and temperature of the occulting atmosphere as well as the uncertainties in these values due to shot noise in the light curve. The derived temperature profiles for immersion and emersion are plotted as a function of number density in Fig. 1. The shaded upper section represents an isothermal atmosphere fit to the initial part of the light curve, which provides definite initial conditions with which to begin the numerical inversion calculation. The inversion was terminated when the uncertainty in the baseline of the light curve produced an error in the temperature equal to the shot noise error. The error bars in Fig. 1 have a total length of two standard deviations, and represent the uncertainty in the overall placement of the profile at that point. The small scale structure is more reliable than the overall placement of the curve because the error in the placement of successive points is strongly correlated^{4,5}.

The fundamental quantity obtained from the inversion is the scale height H which is related to the temperature T of the atmosphere, through the equation $T = \mu g H / R$, where μ is the mean molecular weight of the atmosphere, g is the local gravitational acceleration and R is the universal gas constant. To establish the temperature scales in Fig. 1 we assumed $g = 830 \text{ cm s}^{-2}$ and $\mu = 2.2 \text{ g mol}^{-1}$, which corresponds to an atmosphere of H_2 and He in their solar abundances. If this assumption about the composition is wrong, the scale heights in Fig. 1 will not be affected, but the temperature scales will have an error proportional to the ratio of the true mean molecular weight to that assumed here.

The mean temperature of the inverted section of the profile is 87 K for immersion and 90 K for emersion. The temperature derived by fitting an isothermal atmosphere occultation light curve⁶ to the data is 104 K for immersion and 108 K for emersion. Because the atmosphere is strongly non-isothermal, we feel that the mean inversion temperature should be a more reliable indicator of the mean atmospheric temperature than the isothermal fit temperature.

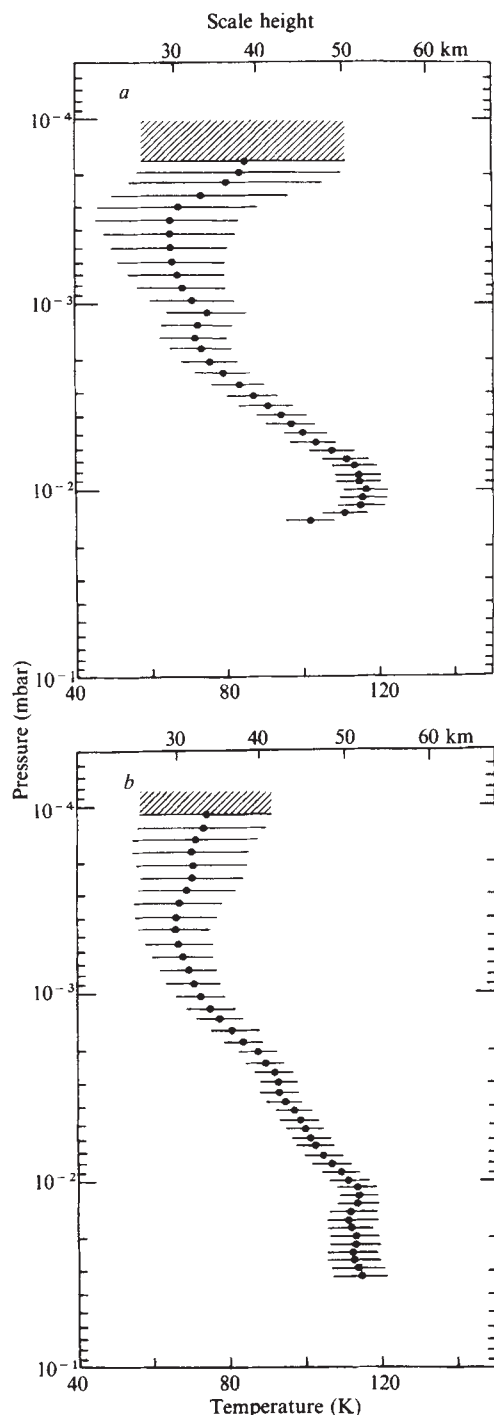


Fig. 1 Temperature profiles of the uranian upper atmosphere for: *a*, 7° N lat, Cape Town immersion; and *b*, 21° S lat, Cape Town emersion. The shaded areas are the regions of the isothermal fit boundary condition. The level at half light is indicated on the right, while the temperature from a full isothermal fit is indicated at the bottom. Note the large variations in temperature.

At the time of the occultation, the subsolar point on Uranus was located at latitude +51.0° and the phase angle was 2.4°. The immersion and emersion points as seen from the Cape were at latitude 7.3° N and 20.9° S respectively, with immersion occurring just before sunrise and emersion just after sunrise. Our results indicate no large difference in the mean temperature for these two conditions.

Both temperature profiles show large variations, ~50 K peak-to-peak for immersion and 40 K for emersion, with a vertical length scale of ~150 km. Although some of this variation is

probably due to noise, we believe that most of these variations represent real temperature variations in the atmosphere of Uranus. First, they are much larger than any variations one might expect from shot noise in the light curve⁴ and second, the profiles agree well with the Kuiper Airborne Observatory (KAO) results^{7,8}. The regions of the uranian atmosphere probed by observations from the Cape and the KAO correspond to the same levels in the atmosphere, but are displaced from each other about 2,200 km along the limb of Uranus for the immersion data and 2,600 km for the emersion data.

The mean atmospheric temperature found here (~90 K) is somewhat cooler than the 140 K found for the upper atmosphere of Neptune from a previous stellar occultation⁹. It is also cooler than that obtained by Wallace¹⁰ from model calculations. Further work will be required to find the reasons for these differences and to establish the cause of the observed 'wavelike' temperature variations. The main problem with dynamical explanations for the wavelike structures is that the obvious wave mechanisms—vertically propagating density waves, for example—apparently heat the atmosphere to much higher mean temperatures than we observed⁸. A more likely possibility is that the variations are caused by photochemical processes⁸.

The data analysis for this work was supported in part by grant AST-7908376 from the NSF. J.C. thanks P. J. Booth for valuable assistance.

Received 13 March; accepted 5 September 1979.

1. Elliot, J. L. *A. Rev. Astr. Astrophys.* **17**, 445 (1979).
2. Taylor, G. E. *J. Br. astr. Ass.* **83**, 352 (1973).
3. Elliot, J. L., Veverka, J. & Millis, R. L. *Nature* **265**, 609 (1977).
4. French, R. G., Elliot, J. L. & Gierasch, P. J. *Icarus* **33**, 186 (1977).
5. French, R. G. & Elliot, J. L. *Astrophys. J.* **229**, 828 (1979).
6. Baum, W. A. & Code, A. D. *Astr. J.* **58**, 108 (1953).
7. Elliot, J. L. & Dunham, E. *Nature* **279**, 307 (1978).
8. Dunham, E., Elliot, J. L. & Gierasch, P. J. *Astrophys. J.* (in the press).
9. Veverka, J., Wasserman, L. & Sagan, C. *Astrophys. J.* **189**, 569 (1974).
10. Wallace, L. *Icarus* **25**, 538 (1975).

Multiply-twinning particles in silver catalysts

L. D. Marks & A. Howie

Cavendish Laboratory, University of Cambridge, Madingley Road, Cambridge, UK

It has been known for several years that anomalous structures can occur in the early stages of particulate growth. Ino¹ and Ino and Ogawa² for gold on rocksalt and Allpress and Sanders³ for nickel on mica found small polycrystalline nuclei which they interpreted as multiply-twinning particles (MTPs). These particles can be considered as 5 or 20 f.c.c. tetrahedra joined by twin boundaries to give decahedra or icosahedra (Fig. 1). As the tetrahedra do not assemble to a completely space filling structure, either elastic strains or grain boundaries are required to complete the particles. More recently, MTPs have been observed in the early stages of growth for all f.c.c. metals in certain conditions. Gillet⁴ has recently reviewed the field whilst Hayashi *et al.*⁵ give extensive results for f.c.c. metals in argon smokes. The possible significance of MTPs in heterogeneous catalysts was first suggested by Allpress and Sanders⁶ and investigated by Avery and Sanders⁷. They found, however, that at most 2% of particles 100–350 Å in size for Ni, Au, Pt and Pd on γ-alumina were multiply twinned. We report here the presence of considerable numbers of multiply-twinning particles in various heterogeneous metal catalysts, in particular silver on α-alumina. The particles can have quite large dimensions up to ~2,000 Å. Attention is drawn to the possible significance of some special sites on these particles which have no counterpart on single crystal surfaces, and to the unusual distribution of surface faces.

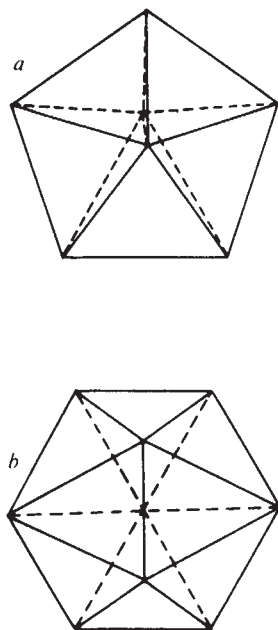


Fig. 1 Structure of *a*, decahedral and *b*, icosahedral multiply-twinned particles.

The samples examined were supplied by ICI Ltd, having been prepared by the following method (UK Patent 1369639): an $0.8 \text{ M}^2\text{g}^{-1}$ support of α -alumina (Carborundum Ltd, No. SAHT96) was immersed in a solution of silver oxalate in 45% water—45% ethylene diamine—10% ethanolamine. The support was then pyrolysed in nitrogen at 200°C for 1 h to decompose the oxalate to silver metal. The catalyst examined contained approximately 16% silver by weight. Samples were prepared for examination in a Siemens 102 microscope by allowing a drop of ground catalyst suspended in acetone to dry on amorphous carbon films premounted on microscope grids.

The samples examined contained principally isolated particles of size between 1,000 and 2,000 Å, although smaller particles (<500 Å) were found associated with amorphous regions of the substrate, and a few large polycrystals were observed, presumably due to particle coalescence. The discrete particles displayed well developed 111 facets, with very little edge or corner rounding. More than 80% of the discrete particles were observed to be MTPs, the remainder being composed mainly of twinned platelets, faulted needles and single crystals. Micrographs of these various morphologies are shown in Figs 2 and 3. All the icosahedral MTPs and most (but not all) of the decahedral MTPs displayed internal contrast suggestive of dislocations, as has been previously noted for large MTPs⁸.

The occurrence of MTPs in heterogeneous catalysts is consistent with their common observation in epitaxial films. MTPs may well occur in many other catalysts; we have, for example, examined micrographs of a nickel catalyst (A. Szczepura, personal communication) which show contrast typical of MTPs. The apparent contradiction between our results and those of Avery and Sanders⁷ is probably due to the different methods of production; the particles described here were prepared by a mild pyrolysis, whereas Avery and Sanders examined their particles after annealing in hydrogen. Preliminary results for <50 Å gold particles on NaCl or amorphous Al_2O_3 have shown that the particles are single crystals after annealing at 500°C in hydrogen but multiply twinned after annealing at 500°C in air. It seems probable that the occurrence and survival of MTPs in catalysts may depend on the atmosphere present during both preparation and running.

The large sizes of the MTPs observed is probably a result of the growth conditions. As the type of particle observed corresponds with the types commonly found for small (<200 Å)

metal particles, it seems likely that the internal structure was determined at some early stage in the growth. Further layer growth, possibly autocatalytic in nature, could produce the observed particles. In the absence of sufficient activation energy from processes such as coalescence, the particles can remain in the multiply twinned structure, even though this is almost certainly metastable in this size range. Given the existence of the multiply twinned structure, the equilibrium of the surface faceting is an additional question. More detailed experimental and theoretical studies of this problem, which will be published elsewhere, suggest that the form observed here, with sharp 111 facets, may in fact be metastable with respect to surface changes at room temperatures and that the stable structure would have additional 100 facets as well as notches at the boundaries.

One interesting feature of the MTP is that they have some unusual surface sites, some of which have no analogue on a single crystal surface. On the actual twin boundary the atoms have h.c.p. coordination rather than f.c.c. so that the *d*-bonds will be differently orientated. Also, as mentioned above, more complicated faceting geometries including notches may arise if the surfaces attain their equilibrium configuration. Such notches or re-entrant surfaces have been considered to act as preferential nucleation sites for crystal growth⁹ and may have some catalytic importance. For a 50-Å radius particle approximately 7% of the surface atoms would be on the twin boundaries, a third of these at the notches.

Anomalous surface sites associated with twins are, of course, also found in other particles. Re-entrant surfaces have been observed for f.c.c. particles with an odd number of closely spaced parallel twin boundaries by Hayashi *et al.*⁵ However, the twin density in MTPs will usually be higher than in other particles.

The fact that MTP surfaces will usually consist of a different distribution of crystal faces than would occur in a single crystal could also be of significance in catalytic reactions which are sensitive to surface crystallography. It seems likely that MTPs will have an anomalously high fraction of their surface as {111} planes and, in addition, the icosahedra will not have any {100} surface planes.

Because the tetrahedral units are not completely space-filling the MTPs probably contain considerable elastic strain, or possibly crystal defects such as dislocations as observed in Si particles by Saito⁸. In either case the catalytic properties may be

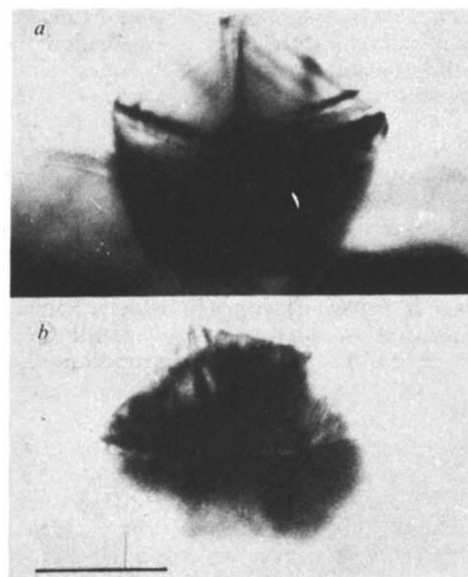


Fig. 2 Micrographs of *a*, Decahedral MTP near the 5-fold symmetry axis and *b*, icosahedral MTP near the 'face' orientation. Scale bar, 0.1 μm .

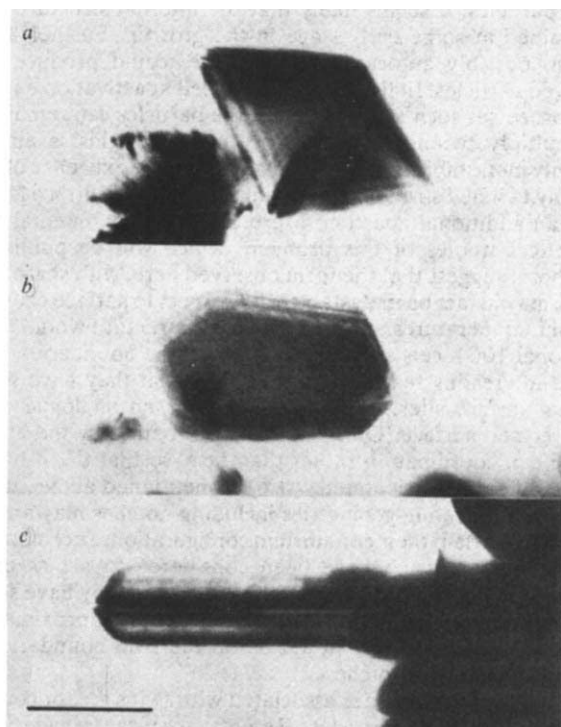


Fig. 3 Micrographs of *a*, single crystal (square pyramid); *b*, platelet and *c*, needle. Scale bar, 0.1 μm .

affected. Ino¹⁰ assumed a homogeneous elastic strain maintained by external forces to estimate the elastic strain energy using anisotropic elasticity theory. His figures for Ag indicate that the lattice parameters in the surface of the icosahedron are expanded by about 3%, while the spacing of planes parallel to the surface is reduced by nearly 5%. The lattice parameter in the surface of the decahedron is increased by 1% in the direction of the $\langle 110 \rangle$ outer perimeter and reduced by 1% in the direction normal to this. Removal of Ino's external forces will lead to additional inhomogeneous elastic strains. De Wit¹¹, for instance, has pointed out the similarity between the decahedron and a disclination which has very high compressions close to the central axis. In the icosahedron the stress is probably also inhomogeneous, being highly compressive at the centre and tensile at the surface. More detailed calculations have been made but these are complicated by the uncertain effects of surface tension stresses in such small particles (A.H., L.D.M. and E. H. Yoffe, in preparation).

Clearly it would be of considerable interest to produce catalyst samples containing, for example, a larger proportion of single crystal particles in the same size range as the MTPs. It might then be possible to make a direct experimental assessment of the practical significance of these anomalous structures in catalysis.

We thank Dr R. W. Clayton (ICI) for supplying catalyst samples and for useful discussions, and the SRC for a CASE Studentship (L.D.M.) and for a grant supporting the electron microscopy of catalysts.

Received 16 July; accepted 27 September 1979.

1. Ino, S. *J. phys. Soc. Jap.* **21**, 346 (1966).
2. Ino, S. & Ogawa, S. *J. phys. Soc. Jap.* **22**, 1365 (1967).
3. Allpress, J. G. & Sanders, J. V. *Surface Sci.* **7**, 1 (1967).
4. Gillet, M. *Surface Sci.* **67**, 139 (1977).
5. Hayashi, T., Ohno, T., Shigeki, Y. & Uyeda, R. *Jap. J. appl. Phys.* **16**, 705 (1977).
6. Allpress, J. G. & Sanders, J. V. *Austr. J. Phys.* **23**, 23 (1970).
7. Avery, N. R. & Sanders, J. V. *J. Catal.* **18**, 129 (1970).
8. Saito, Y., Yatsuya, S., Mihama, K. & Uyeda, R. *Jap. J. appl. Phys.* **17**, 1149 (1978).
9. Frank, F. C. *Discuss. Faraday Soc.* **5**, 48, 186 (1949).
10. Ino, S. *J. phys. Soc. Jap.* **27**, 941 (1969).
11. De Wit, R. *J. Phys. C* **5**, 529 (1972).

Propagating chemical waves in the uncatalysed gallic acid–bromate system

K-W. Pehl, L. Kuhnert & H. Linde

Zentralinstitut für physikalische Chemie, Akademie der Wissenschaften der DDR, 1199 Berlin, Rudower Chaussee 5–6, DDR

Chemical oscillatory systems which include at least one autocatalytic reaction step are of interest as thermodynamically open systems in which temporal and spatial structures are produced. These systems also show other types of unusual kinetic behaviour¹. To analyse the elementary steps of their kinetics the simplest possible reactions are needed especially in relation to nonlinear thermodynamics². The theory of these chemical reactions is still only at the level of a simplified mathematical model, and theoretical results are in poor agreement with experimental findings. Therefore it is important to study other examples of spatial dissipative structures corresponding to chemical systems which exhibit oscillations. We report here observations of the oscillating reaction between bromate and the phenolic compound gallic acid in which propagating chemical waves occur.

The Belousov–Zhabotinskii reaction system (BZR) is known to exhibit propagating chemical waves³. This reaction is very complex and involves about 20 elementary steps (the mechanism has been elucidated by Field *et al.*⁴) starting from an initially homogenous state. Until now no other chemical reaction starting from this condition has been found to form a spatial structure spontaneously (unlike a Liesegang ring-type one).

The BZR requires a transition metal catalyst but the rate law of wave propagation shows the propagation velocity to be independent of the concentration of the catalyst in the range studied by Noyes and Field⁵. This means that the step catalysed by the transition metal ion, although necessary for oscillation and/or wave propagation in the BZR does not determine the propagation velocity.

Körös and Orban⁶ have reported a new oscillatory chemical reaction between bromate and phenolic or aniline-type compounds, occurring in the absence of a catalyst. (A catalyst may be added, but the reaction then becomes of the normal BZR type^{7,8}.) A similar reaction between bromate, and bisazonium salts was reported previously by Kuhnert and Linde⁷.

Our experiments were carried out at room temperature in Petri dishes using a solution volume of 11 ml to give a layer ~1 mm deep. As the waves were hardly visible in daylight, they were observed and photographed under filtered blue light from a high-pressure mercury discharge lamp. The light intensity selected was low enough to prevent photochemical excitation of the reaction mixtures (formation of bubbles).

The reaction solutions were prepared in the following way. Mixtures of 7 ml of distilled water, 3 ml of sulphuric acid (4 M), and 1 ml of a solution of sodium bromate (1.5 M), were stirred and saturated with gallic acid; excess gallic acid was filtered off rapidly, and the filtrates were poured into Petri dishes. Reaction times were measured from when components were mixed. The brown solutions rapidly turned pale but darkened again slowly. After periods of 3 to 10 min colourless waves started propagating with a speed of 2 to 4 mm per minute from leading centres commonly situated at the borders of the dishes. In most experiments several leading centres appeared, and when the waves propagating from them came into contact, destructive interference was observed. Artificial leading centres could be created by adding droplets of concentrated sodium bromate solution to the reaction mixtures, these leading centres exhibited the same behaviour as the original ones, but often generating waves of shorter wavelength. Wave propagation was generally

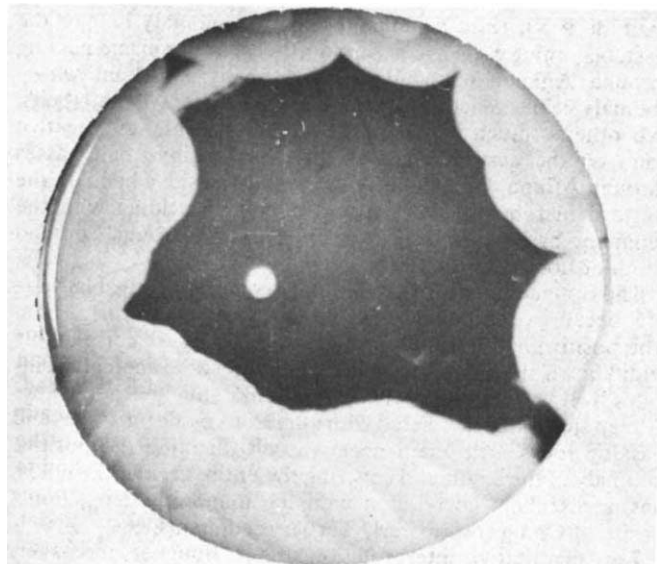


Fig. 1 Wave propagation in the uncatalysed gallic acid–bromate system. The diameter of the Petri dish is 100 mm. Concentrations (molar): H_2SO_4 , 1.09; NaBrO_3 , 0.136; gallic acid, ~ 0.04 (saturated solution). The reaction time of the mixture was 12 min 20 s. To avoid reflections, the dish was uncovered while the photograph was taken.

observed for periods of about 30 min, the waves fading slowly.

In several cases spatial irregularities were observed at the beginning of the reaction: areas not yet reached by a wave front suddenly showed an irregular colour change propagating about 10 times faster than wavefronts. This effect disappeared as soon as a wavefront reached these areas. The same effect was reported by Zaikin and Zhabotinskii³. We assume this effect to be a pseudo-wave which propagates much faster than ordinary trigger waves, and which appears only where trigger waves have not yet started propagating⁹.

There has been some controversy as to whether those leading centres (also called pacemakers) from which the waves propagate may appear spontaneously. It arose because Winfree¹⁰ assumed that in the BZR leading centres were caused by dust particles or similar heterogeneities of the system. Note that the general theory of irreversible thermodynamics forces an amplification of fluctuations in the system. An oscillatory reaction involves autocatalytic steps which are able to amplify such fluctuations.

Zaikin and Kawczynski¹¹ developed a theory to explain this effect. They distinguished between the pacemaker and the leading centre. The pacemaker is caused by a permanent local heterogeneity (such as a dust particle), whereas the leading centre can only be produced by an initial perturbation of concentration or phase. It would be very difficult to exclude completely all impurities, such as dust particles, and impurities may constitute a much greater potential disturbance of the homogeneity of the system than the fluctuations under study. Thus a macroscopic heterogeneity might be expected to trigger waves more effectively than can fluctuations. Similar earlier controversies concerned the oscillatory behaviour of the Bray–Liebhafsky reaction which was thought to be caused by gas bubbles.

We have given an additional example showing that a well defined macroscopic concentration gradient can also trigger chemical waves. It should be emphasised, however, that even when all impurities were excluded as far as possible wave propagation started spontaneously. Presumably the induction and synchronisation of the temporal and spatial phase difference in the propagating wave took a longer time in this case. The pseudo wave seems to be an early step in the development of this process.

The brown colour observed is probably caused by oxidative formation of a semiquinone compound from gallic acid, but the precise reactions that make up this oscillatory reaction system are not yet known.

Received 10 April; accepted 6 August 1979.

1. Franck, U. F. *Agnew. Chem.* **90**, 1–16 (1978).
2. Glansdorff, P. & Prigogine, I. *Thermodynamic Theory of Structure, Stability, and Fluctuations* (Wiley-Interscience, New York, 1971).
3. Zaikin, A. N. & Zhabotinskii, A. M. *Nature* **225**, 535–537 (1970).
4. Field, R. J., Körös, E. & Noyes, R. M. *J. Am. chem. Soc.* **94**, 8649–8664 (1972).
5. Field, R. J. & Noyes, R. M. *J. Am. chem. Soc.* **96**, 2001–2006 (1974).
6. Körös, E. & Orban, M. *Nature* **283**, 371–372 (1978).
7. Kuhnert, L. & Linde, H. Z. *Chem.* **17**, 19–20 (1977).
8. Sreekantha Babu, I. & Srinivasulu, K. Z. *phys. Chem. Leipzig* **259**, 1191–1195 (1978).
9. Winfree, A. T. *Lecture Notes in Biomathematics*, Vol. 2 (Springer, Berlin, 1974).
10. Winfree, A. T. *Science* **175**, 634–636 (1972).
11. Zaikin, A. N. & Kawczynski, A. L. *J. Non-Equilib. Thermodynam.* **2**, 39–48 (1977).

Gravity field of Benue Trough, Nigeria

Chris Adighije

Geology Department, University of Ibadan, Ibadan, Nigeria

The Benue Trough, located at the Gulf of Guinea re-entrant on the West African coast (Fig. 1), is a unique Cretaceous rift whose origin is related to the opening of the South Atlantic and the continental separation of Africa from South America. The trough extends northeastwards for ~ 700 km from the Niger Delta to the Chad Basin and is filled with an estimated 5,000 m of Cretaceous sediments and volcanic rocks. Studies on the origin and tectonic evolution of the Benue Trough have been based so far principally on surface geological and geochemical evidence^{1–5}. Gravity measurements by Cratchley and Jones⁶ in the middle Benue area are of limited significance because they were aimed mainly at resolving the then controversy between the tensional and compressional⁸ hypotheses. New and more extensive gravity data presented here indicate rifting in the upper and middle sections of the trough whereas the complex field over the lower section could be due to an ‘unsuccessful’ attempt to open into an ocean during the late Cretaceous.

Six hundred additional gravity measurements were made at 2–10 km spacings along passable roads (in the lower and upper areas of the trough) to fill up earlier gaps in information⁹. A Canadian Scintrex CG-2 gravimeter No. 305G, with a repeat accuracy of 0.01 mGal and average drift of 0.06 mGal h^{-1} , was used in measuring the gravity values. About 20% of the gravity stations were located on known elevation bench marks; elevations of other stations were determined by using a single Paulin system altimeter in loops of up to 2-h duration. These elevations have an estimated error of ± 15 m. Station positions which have been established on a 1:1,000,000 scale map are correct to ± 500 m. Free-air, Bouguer, terrain and latitude corrections were applied to the observed gravity values. The maximum possible error of the final Bouguer anomaly values is estimated to be about ± 3 mGal.

Figure 2 is the resulting Bouguer contour map with relative gravity values ranging from -60 mGal near Kaltungo to $+20$ mGal near Abakaliki. Generally the Bouguer values decrease towards the flanking basement complex areas; for example, the value near Jos (Younger Granite province) is -90 mGal (ref. 9). Two distinct regions can be easily identified: (1) a positive gravity anomaly belt whose axis begins from south of Ishiagu, reaches $+20$ mGal near Abakaliki and terminates near Gboko. Beyond Gboko, the positive anomaly becomes much smaller in magnitude and disappears near south of Zurak

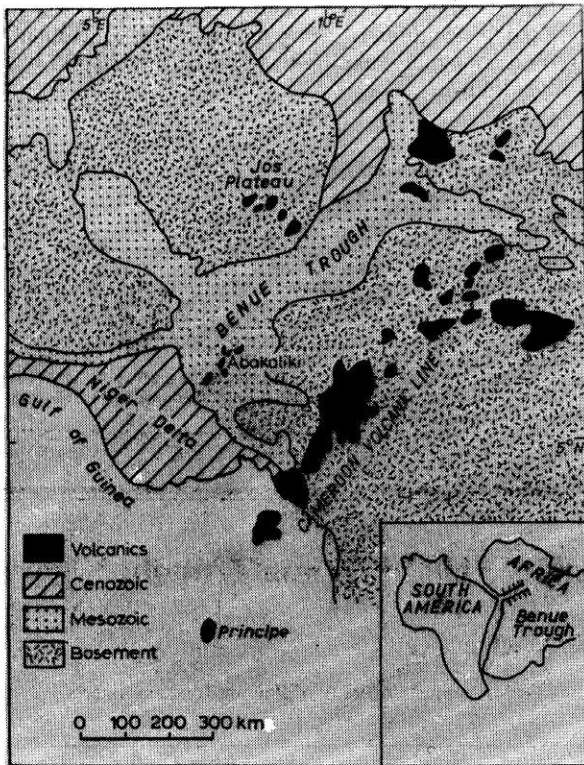


Fig. 1 Location map of Benue Trough.

(latitude 9°N); (2) a prominent negative anomaly belt to the west, beginning with -40 mGal south-east of Benin and passing through Ankpa, Wase, Wikki and finally Potiskum where anomaly values reach -60 mGal. Besides these two main belts, two others—much less defined—are discernible. A negative band on the eastern flank of the main positive belt passes through Afikpo, Ogoja and Wukari, and a positive band on the western margin of the map and almost coinciding with the sediment-basement boundary can be traced through Ore and south of Lokoja to Shendam.

The Bouguer map is relatively more complex south of latitude 9°N because of the complex geological structure of this region. The positive and negative Bouguer anomalies are correlatable with known surface geology; the belt of positive anomaly coincides well with the core of the Abakaliki anticlinorium where Albian shales are associated with numerous mafic intrusives and basaltic rocks. The main negative belt, flanking the positive anomaly in the south and covering the entire area in the north, has an excellent correlation with the numerous depositional basins of Cretaceous to early Tertiary sediments.

For quantitative interpretation of the Bouguer anomalies, four profiles (AA', BB', CC', DD') across the trough were selected (Fig. 2). The most outstanding feature of the profiles is a regional positive anomaly over the whole trough floor (Fig. 3). The profiles of the regional anomaly display striking similarity with one another, suggesting a deep-seated structure of considerable extent along the trough. Each profile in Fig. 3 also shows the uplift in the Moho boundary that would cause the gravity regional (with a mantle-crust density contrast of 0.57 g cm^{-3}). The mantle-crust interface (Moho) thus seems to have been elevated by ~1.5 km in the Lower Benue

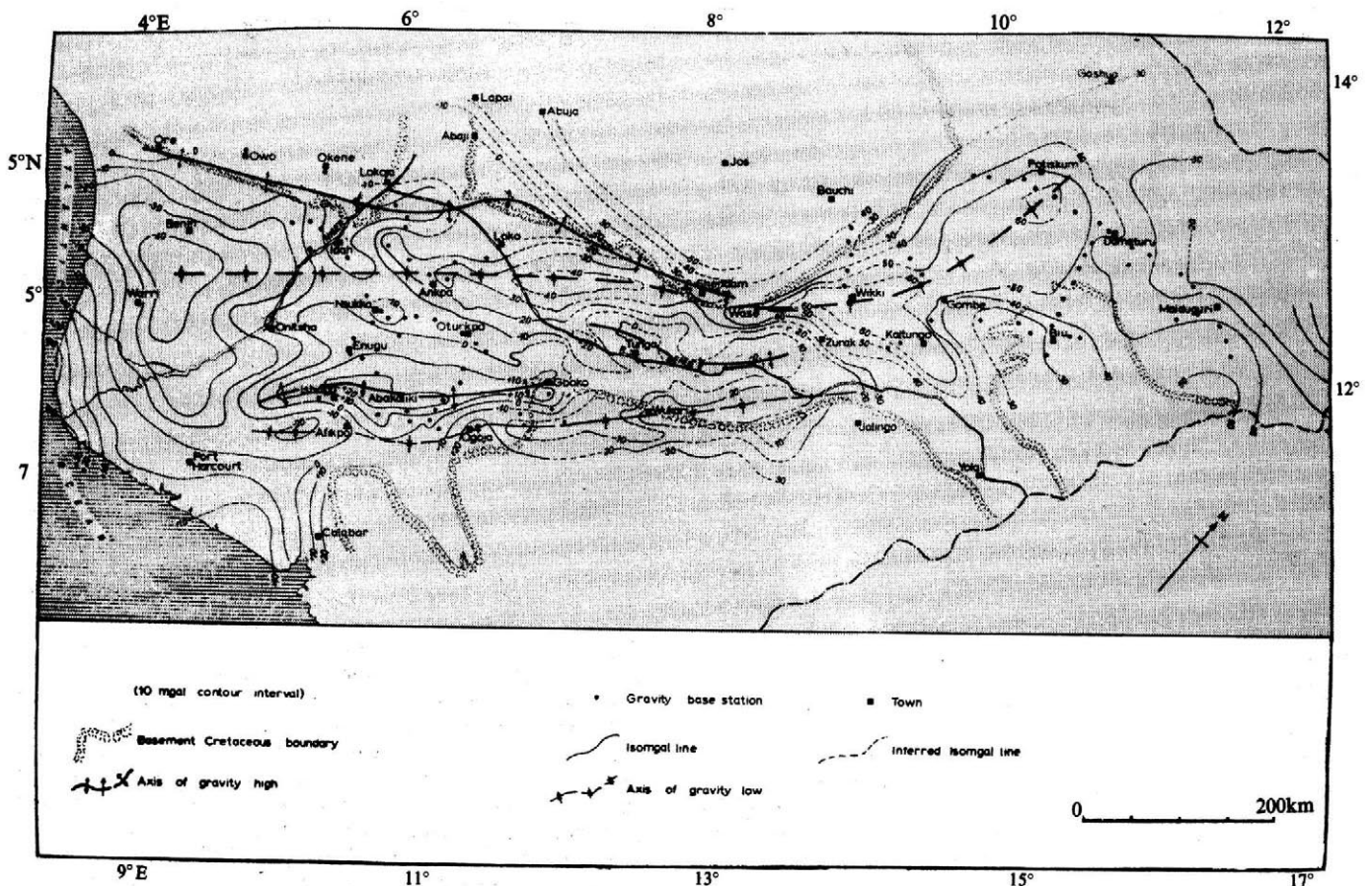


Fig. 2 Bouguer anomaly map of Benue Trough.

and ~3.0 km in the Upper. On the other hand, the width of the Moho uplift decreases from 170 km in the Lower to 70 km in the Upper Benue.

The residual positive anomaly belt from Abakaliki to Gboko has been interpreted as a two dimensional body of density 2.90 g cm^{-3} , average width of 30 km, and extending from a depth of 10 km down to the Moho (Fig. 4).

Uplifting of the Moho beneath rift structures has also been observed in other regions—Kenya Rift Valley¹⁰, Gulf of Suez¹¹, Red Sea¹², Baikal Rift¹³ and Oslo Graben¹⁴. Artsybashev and Kogbe¹⁵ had previously obtained a rather high value, 10–12 km, for the mantle uplift in Middle Benue. This is primarily due to their use of too small a value for the mantle–crust density contrast, namely, 0.17 g cm^{-3} , as against the 0.57 g cm^{-3} used

here. The relatively small mantle uplift, as obtained in this study, could relate to the fact that the Benue Rift became inactive during the late Cretaceous following the rotation of the African plate and the consequent shift of tectonic activity to the Cameroun volcanic line⁵.

The shape and size of the high density material that generates the main positive anomaly belt (Abakaliki–Gboko) is shown in Fig. 4. This anomalous body can hardly be considered as an intrusive because of its very large dimensions. It rather resembles a 'mantle diapir' which, in turn, might have been the source of the volcanic rocks in the area.

The negative anomalies which flank the positive belt in the south, and form the axial plane in the north, are considered to be due entirely to the sediments that fill the Benue Trough. The

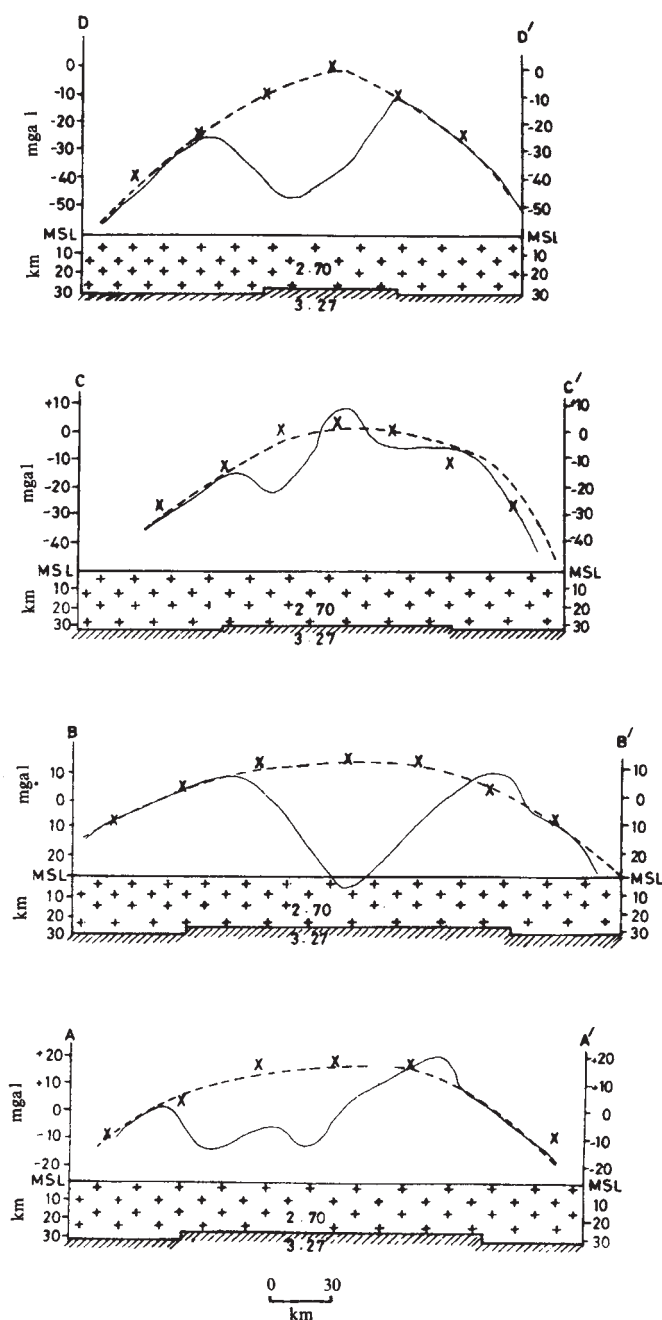


Fig. 3 Calculated regional anomaly for crustal models along profiles AA'–DD'. Solid line, observed gravity; dashed line, regional anomaly; x, calculated anomaly due to the regional model.

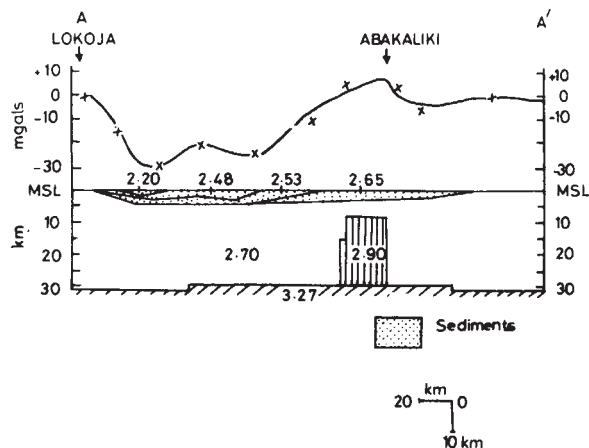


Fig. 4 Calculated residual gravity anomaly for model along profile AA'. Solid line, residual anomaly; x, calculated anomaly.

maximum thickness of sediments in the Lower Benue area was calculated as 4,250 m (Fig. 4). In the Upper sections a maximum thickness of 6,000 m has been obtained⁶.

The results of this study are consistent with a tensional origin related to the opening of the South Atlantic. The gravity anomaly patterns in the upper and middle sections of the trough are similar to those of other sediment-filled rifts. The complexity of the gravity field in the Lower Benue can be attributed to its proximity to the hotspot and triple junction which was beneath the present Niger delta. This was associated with an unsuccessful attempt to open the Benue Trough into an ocean during the late Cretaceous.

I thank H. Higashinaka for support and M. A. Olade and A. Roy for useful discussions. Computer models were calculated at University of Birmingham, UK. Fieldwork was financed by grants from the University of Ibadan.

Received 2 May; accepted 24 August 1979.

1. Wright, J. B. *Tectonophysics* **6**, 301–310 (1968).
2. Grant, N. K. *Bull. geol. Soc. Am.* **82**, 2295–2298 (1971).
3. Burke, K., Dessauvage, T. F. J. & Whiteman, A. J. *Nature* **233**, 51–55 (1971).
4. Nwachukwu, S. O. *Geol. Mag.* **109**, 411–419 (1972).
5. Olade, M. A. *Geol. Mag.* **112**, 575–583 (1975).
6. Cratchley, C. R. & Jones, G. P. *Overseas Geol. Surv. Geophys. Pap. I* (1965).
7. King, L. C. *Geol. Mag.* **87**, 553–359 (1950).
8. Lees, G. M. Q. *J. geol. Soc. Lond.* **108**, 1–34 (1952).
9. Ajakaiye, D. E. & Burke, K. C. *Tectonophysics* **16**, 90–103 (1973).
10. Searle, R. C. *Geophys. J. R. astr. Soc.* **21**, 13–31 (1970).
11. McKenzie, D. P., Davies, D. & Molnar, P. *Nature* **226**, 3243–3248 (1970).
12. Qureshi, I. R. *Geophys. J. R. astr. Soc.* **24**, 110–135 (1971).
13. Lubimova, E. A. *Tectonophysics* **8**, 457–467 (1969).
14. Ramberg, I. B. & Smolthson, S. B. *Tectonophysics* **11**, 419–431 (1971).
15. Artsybashev, V. A. & Kogbe, C. A. *Geol. Rdsch.* **64**, 324–429 (1974).

Evidence for organically associated iron in nearshore pore fluids

Wm. Berry Lyons, Henri E. Gaudette
& Peter B. Armstrong

Department of Earth Sciences
and Ocean Processes and Analysis Laboratory,
University of New Hampshire, Durham, New Hampshire 03824

The role of dissolved organic matter (DOM) in the speciation of trace metals in natural waters is poorly understood¹⁻³. Although dissolved organic matter-iron associations have been observed in freshwater systems⁴⁻⁶, it has been thought that DOM-iron species are not significant in saline waters⁷. Yet recent studies have suggested that iron-DOM interactions in the pore waters of anoxic marine sediments may be important^{8,9}. The possibility of organically associated trace metals in anoxic water has been used to explain why metal concentrations are higher than those predicted by sulphide-mineral equilibria^{10,11}. We present here data that indicate that strong iron-DOM associations do occur in the anoxic pore waters of nearshore marine sediments and that both the total dissolved iron and organically associated iron change seasonally.

Five box cores were taken within 1 m² of each other between February and September 1978, in a subtidal area in the Great Bay estuary, New Hampshire. The cores were treated very carefully so that the sediment and its pore fluid would not be exposed to the atmosphere at any time. In the laboratory the corer was placed in a nitrogen-filled glove bag, extruded, sectioned into 2-cm sections, centrifuged and filtered through precleaned 0.4- μ m membrane filters. Details on handling and cleaning procedures are published elsewhere^{12,13}. The inert atmosphere was maintained to minimise oxidation artefacts¹⁴⁻¹⁶. While in the glove bag, the filtered pore water samples were separated into two aliquots and one acidified to pH ~1 with ultrapure HNO₃ and the other acidified to a pH of ~2.8 with ultrapure HCl. The HNO₃ acidified samples were then placed into a water bath at 90 °C, heated for 1 h and analysed for total dissolved iron using the technique of Murray and Gill¹⁷. The HCl acidified samples were passed through a column of the macroreticular resin, Amberlite XAD-2, utilising the flow parameters outlined by Mantoura and Riley¹⁸. This resin has been shown to be very efficient in removing humic substances from natural water samples of pHs between 2 and 3 (refs 19-21). Due to the harshness of this procedure (acidification), the Amberlite extractable iron fraction should be considered as iron that is very strongly associated with the humic material present in the pore fluids. Sugimura *et al.*²² have shown, however, that 80-90% of the total iron present in seawater is removed by

procedures similar to those outlined above. Only 10% of the total iron is removed by the resin if the sample is not previously acidified. This technique probably underestimates the iron that is actually associated by pore water DOM. The resin was eluted with ultrapure 1M NaOH, acidified to pH ~1 with ultrapure HNO₃, heated in the water bath for 1 h and analysed for 'humic-substance associated iron' or organic iron. The standard deviation of the iron measurements reported as a coefficient of variation was 2% at 10 μ mol⁻¹ and 10% at 2 μ mol⁻¹. The data are shown in Table 1.

The total dissolved iron values proceed through a seasonal cycle with the highest concentrations observed in the late spring and the lowest in mid-summer. This seasonal cycle of dissolved Fe can be correlated with bacterial cycling of sulphur and DOM in these sediments²³. In the spring, as the temperature of the water and the sediment increases, anaerobic fermenting bacteria begin to metabolise at a faster rate producing reduced end-products which lower the sediment Eh. As the Eh is lowered more Fe³⁺ is solubilised to Fe²⁺ in the pore waters. Bacterially mediated sulphate reduction occurs as the temperature increases and the Fe present in the pore fluids in the late spring is removed by mid-summer by the *in situ* formation of FeS. Similar seasonal pore cycling of Fe has recently been observed in temperate salt marsh sediments²⁴.

The May samples also have the highest percentages of organic iron in the pore waters, with an average of 31% of the total iron being organically associated. This compares with 10% or less for the other sampling dates. It thus seems that the production and removal of this organic-iron fraction is strongly related to sedimentary microbial dynamics. Laboratory experiments have shown that the pigment and lipoidal fractions (1,500-50,000 molecular weight fraction) of DOM from the bacterial degradation of algae can form water soluble iron-organic associations²⁵. It has been suggested that a syntrophic relationship exists between fermenting and sulphate reducing bacteria and that fermenting bacteria produce organic substrate for subsequent sulphate reducing bacterial growth²⁶. Although our conclusions are based on a single set of samples from one site, it seems that this interaction between bacterial groups may also have a profound effect on trace metal speciation in anoxic waters.

We thank Bill Orem for his help in obtaining the samples, Mark Hines for reviewing the original manuscript and Jon Kim for help in reviewing the literature. This work was supported by NSF grant OCE77-20484 and Sea Grant 04-8-MOI-79.

Received 20 June; accepted 12 September 1979.

1. Reuther, J. H. & Perdue, E. M. *Geochim. cosmochim. Acta* **41**, 325-334 (1977).
2. Pocklington, R. *Mar. Chem.* **5**, 479-496 (1977).
3. Lyons, W. B. & Fitzgerald, W. F. *Geochim. cosmochim. Acta* (submitted).
4. Schindler, J. E., Alberts, J. J. & Honick, K. R. *Limnol. Oceanogr.* **17**, 952-957 (1972).
5. Sholkovitz, E. *Geochim. cosmochim. Acta* **40**, 831-845 (1976).
6. Perdue, E. M., Beck, K. C. & Reuther, J. H. *Nature* **260**, 418-420 (1976).
7. Kester, D. R., Byrne, R. H., Jr & Liang, Y.-J. in *Marine Chemistry in the Coastal Environment* (ed. Church, T. M.) 56-79 (Am. chem. Soc., Washington, D.C., 1975).
8. Nissenbaum, A. & Swaine, D. J. *Geochim. cosmochim. Acta* **40**, 809-816 (1976).
9. Krom, M. D. & Sholkovitz, E. R. *Geochim. cosmochim. Acta* **41**, 1565-1573 (1977).
10. Spencer, D. W. & Brewer, P. G. *J. geophys. Res.* **76**, 5877-5892 (1971).
11. Presley, B. J., Kolodny, Y., Nissenbaum, A. & Kaplan, I. R. *Geochim. cosmochim. Acta* **36**, 1073-1090 (1972).
12. Contreras, R., Fogg, T. R., Chasteen, N. D., Gaudette, H. E. & Lyons, W. B. *Mar. Chem.* **6**, 365-373 (1978).

Table 1 Pore water concentration of total dissolved iron and organically associated iron from Great Bay, New Hampshire

Depth (cm)	10 February		27 March		Fe (μ mol ⁻¹) 9 May		20 July		22 Sept 78	
	Total	Organic	Total	Organic	Total	Organic	Total	Organic	Total	Organic
1	50	<1	39	1	220	50	<1	<1	54	2
3	—	—	50	2	119	15	<1	<1	21	2
5	100	1	19	3	101	20	<1	<1	10	1
7	69	8	18	1	40	10	<1	<1	1	<1
9	34	3	8	1	37	10	<1	<1	3	<1
11	12	2	8	1	9	7	<1	<1	2	<1

All measurements were taken in 1978.

13. Lyons, W. B., Gaudette, H. E. & Hewitt, A. D. *Geochim. cosmochim. Acta* **43**, 433–437 (1979).
14. Troup, B. N., Bricker, O. P. & Bray, J. T. *Nature* **249**, 237–239 (1974).
15. Loder, T. C., Lyons, W. B., Murray, S. & McGuinness, H. *Nature* **273**, 373–379 (1978).
16. Lyons, W. B., Gaudette, H. E. & Smith, G. M. *Nature* **277**, 48–49 (1979).
17. Murray, J. W. & Gill, G. *Geochim. cosmochim. Acta* **42**, 9–19 (1978).
18. Mantoura, R. F. C. & Riley, J. P. *Analyt. chim. Acta* **76**, 97–106 (1975).
19. Stuermer, D. H. & Harvey, G. R. *Nature* **250**, 480–481 (1974).
20. Mantoura, R. F. C., Dickson, A. & Riley, J. P. *Est. Coast. mar. Sci.* **6**, 387–408 (1978).
21. Sugimura, Y., Suzuki, Y. & Miyake, Y. *Deep-Sea Res.* **25**, 309–314 (1978).
22. Sugimura, Y., Suzuki, Y. & Miyake, Y. *J. oceanogr. Soc., Jap.* **34**, 93–96 (1978).
23. Lyons, W. B., Gaudette, H. E., Armstrong, P. B. & Orem, W. H. *Abstr. 42nd A.S.L.O. Meet., Corpus Christi, Texas* (1979).
24. Lord, C. J. & Church, T. M. *Trans. Am. geophys. Un.* **60**, 293 (1979).
25. Akiyama, T. *Geochim. J.* **7**, 167–177 (1973).
26. LeGall, J. & Postgate, J. R. in *Advances in Microbial Physiology*, Vol. 10 (eds Rose, A. H. & LeGall, J.) 81–133 (Academic, New York, 1973).

Cell-surface labelling reveals no evidence for membrane assembly and disassembly during fibroblast locomotion

C. A. Middleton

Department of Anatomy, School of Medicine,
The University of Leeds, Leeds, UK

As a cultured fibroblast moves, particles or pieces of debris attached to its surface move backwards with respect to both the cell and the substrate^{1,2}, as also do concanavalin A (Con A) receptors in the membrane of the leading lamella³. One suggested explanation is that membrane components from the cytoplasm are assembled and introduced into the surface membrane of the moving cell close to its leading edge and flow backwards to a 'sink'; there the membrane is disassembled, and its components enter the cytoplasm and flow forward within the cell, to be re-introduced later into the surface membrane^{1,4}. However, because cell-surface receptors can be redistributed as a result of cross-linking by external ligands^{5,6} it has been proposed that the backward flow of Con A receptors and particles may result from such a cross-linking rather than from a flow of intact cell membrane^{7,8}. To investigate these alternatives, I have studied moving fibroblasts by means of a cell membrane label that does not induce the redistribution of its receptors. My results do not seem compatible with the membrane flow model.

The Thy-1.1 alloantigen (formerly Θ AKR) is an integral membrane glycoprotein originally identified on mouse T lymphocytes⁹ and also found on fibroblasts from Wistar-Furth (W/Fu) rats^{10,11}. Treatment of lymphocytes¹² and W/Fu fibroblasts (C.A.M., unpublished observations) with alloantisera directed against this alloantigen (anti-Thy-1.1) does not result in the redistribution of the antigen. This does not imply, however, that the antigen is anchored in the membrane, for in lymphocytes¹², and both suspended and spread W/Fu fibroblasts (C.A.M., unpublished observations), incubation with an additional layer of antibody directed against anti-Thy-1.1 will induce the redistribution of the antigen into patches and caps.

Cultured rat W/Fu fibroblasts were cooled rapidly to inhibit locomotion and incubated with mouse anti-Thy-1.1 in the cold. The cells were then returned to 37°C and the locomotion of a selected cell was filmed: ruffling and locomotory activity of the cells was unaffected by incubation with anti-Thy-1.1. The cells were again cooled to prevent further locomotion, and before fixation were incubated with fluorescein-conjugated rabbit anti-mouse IgG (anti-MIg-Fl) to make possible visualisation of the anti-Thy-1.1 (details in Fig. 1). The selected cell was then observed by incident light fluorescence microscopy.

When there was no incubation at 37°C, so that cells were unable to move between treatments with the two antisera, there was an even distribution of fluorescent label (Fig. 1), indicating

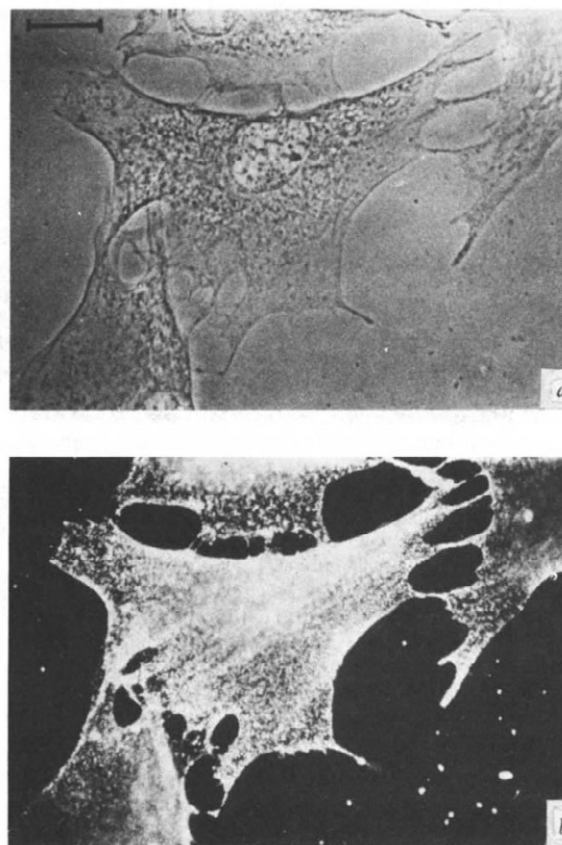


Fig. 1 Fluorescent labelling of Thy-1.1. Fibroblasts were initially obtained as contaminants of myoblast cultures from neonatal W/Fu rats. They were subsequently maintained by twice weekly subculture in Dulbecco's modified Eagle's medium (MEM) containing 10% fetal calf serum (FCS, Flow Labs), penicillin (100 IU ml⁻¹) and streptomycin (100 µg ml⁻¹). When required, cells were collected and adjusted to a concentration of 5×10^3 ml⁻¹ in medium as above, and 1-ml aliquots of this suspension were plated out on to 13-mm diameter glass coverslips contained within Linbro multidish wells (16 mm diameter, Flow Labs). The coverslips had previously been marked, using Indian ink, with a reference grid of side approximately 2 mm to allow the subsequent localisation and identification of selected cells. After 24 or 48 h culture, a selected coverslip was cooled rapidly by washing in HEPES-buffered MEM (MEM-H) containing 20% FCS at 4°C and then incubated in anti-Thy-1.1 (1:4) prepared as described by Raff¹⁸ for 30 min at 4°C. The coverslip was then thoroughly washed in MEM-H at 4°C and maintained in MEM-H plus 10% FCS at 4°C, and a suitable cell selected. The cold medium was then replaced with MEM-H plus 10% FCS prewarmed to 37°C and the selected cell was filmed under phase contrast optics by time-lapse cinematography (1 frame per 3 s) for 15–180 min. At the end of the period of filming, the culture was rapidly cooled by washing in MEM-H plus 20% FCS at 4°C and then incubated in anti-MIg-Fl (1:10, Miles Labs) for 30 min at 4°C. After thorough washing in MEM-H at 4°C, the culture was fixed in absolute methanol for 2 min and mounted in phosphate-buffered saline. The culture was examined using a Leitz Orthoplan microscope equipped with phase contrast and incident light fluorescence optics suitable for fluorescein fluorescence. The filmed cell was re-identified using the reference grid and paired phase contrast and fluorescence micrographs obtained. *a*, *b*, Distribution of fluorescence on control cells. The period of locomotion at 37°C was eliminated from the above protocol by maintaining the cells at 4°C throughout; incubation with anti-Thy-1.1 was followed immediately by washing and incubation with anti-MIg-Fl. A group of cells was photographed with phase contrast optics (*a*) and with incident light fluorescence optics (*b*). Scale bar, 20 µm.

an even distribution of Thy-1.1 over the surface of the cell. Fluorescent labelling was prevented if there was no incubation with anti-Thy-1.1.

Figure 2 shows an experiment in which a selected cell was filmed for 30 min at 37°C after incubation with anti-Thy-1.1. The cell ruffled during filming and stills taken from the first (Fig. 2*a*) and last (Fig. 2*b*) frames of the film show that regions of the leading lamella advanced up to 30 µm (Fig. 2*c*). Treatment with anti-MIg-Fl showed that the distribution and intensity of the

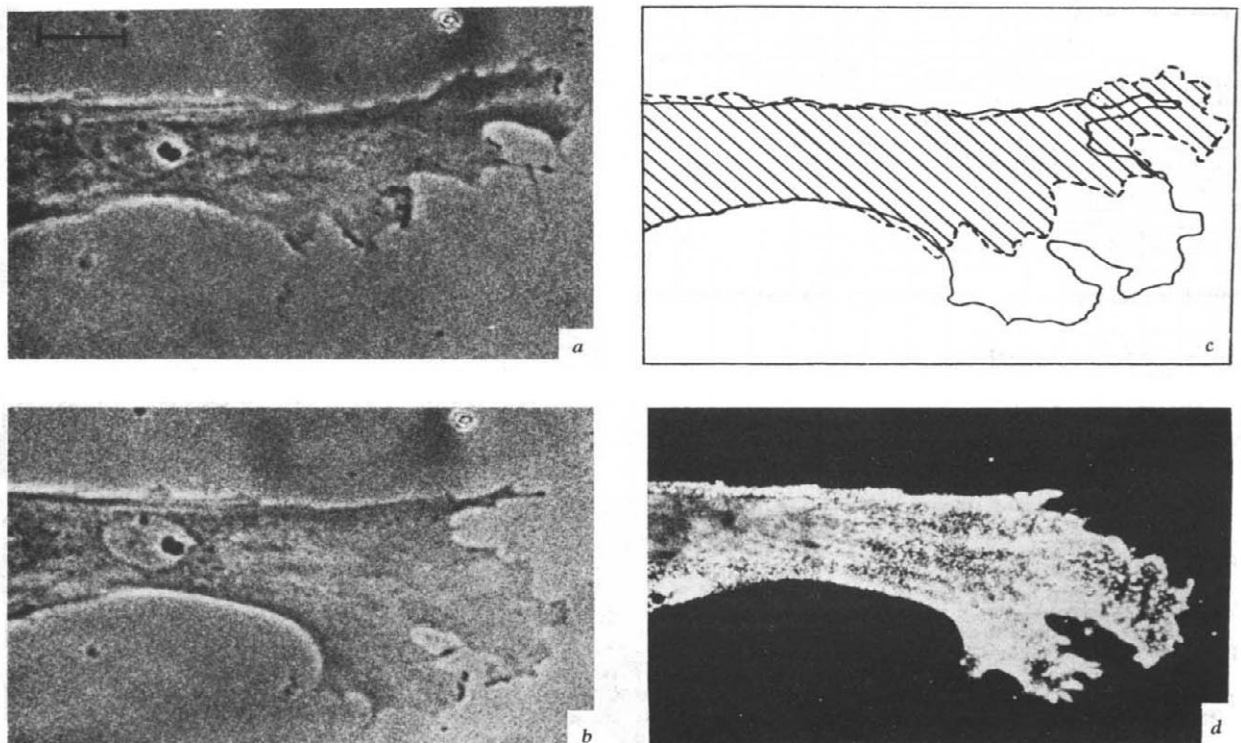


Fig. 2 Distribution of fluorescence on a fibroblast after locomotion. The method used was as described in Fig. 1 legend, the selected cell being filmed for 30 min at 37 °C after incubation with anti-Thy-1.1 and before incubation with anti-Mlg-FI. *a*, *b*, Stills taken from the time-lapse film at the start of filming (*a*) and at the end of filming (*b*); *c*, superimposition of tracings from *a* and *b* to show the movement of the cell; *d*, fluorescence micrograph of the same cell. Scale bar, 20 μ m.

fluorescent labelling (Fig. 2*d*) were indistinguishable from that on control cells which had not moved (compare Figs 1*b* and 2*d*). Similar experiments in which the cells moved for 15–180 min after incubation with anti-Thy-1.1 antiserum yielded identical results.

Con A labelling experiments had suggested a coordinated backward flow of newly assembled membrane from the leading edge of the cell³, but my results are incompatible with that. If membrane were assembled during the period of locomotion, the newly assembled membrane would contain Thy-1.1 previously within the cytoplasm, unavailable to the anti-Thy-1.1 and therefore not detectable by anti-Mlg-FI. A coordinated backward flow of newly assembled membrane would therefore appear as a gradual retreat of fluorescent label from the leading edge, because, with increasing time, more and more membrane containing Thy-1.1 unavailable for subsequent labelling would be introduced at the leading edge of the cell. There was no sign of such a retreat.

Although my results argue against coordinated backward flow of the membrane, some less organised flow may be possible because membrane components, both protein and lipid, are free to diffuse in the plane of the membrane (see ref. 6 for review), and so components inserted during locomotion might be expected to mix with those already present on the cell surface. In my experiments any Thy-1.1 inserted during locomotion is unavailable for subsequent labelling (see above). This will mix with and dilute the Thy-1.1 already present on the surface and available for labelling at a rate largely determined by the speed of membrane assembly and disassembly. This dilution would be detected as a gradual decrease, with time, in the intensity of subsequent labelling. Studies of particle movements during fibroblast locomotion suggested that the membrane was being

assembled and disassembled at a rate equivalent to replacing the entire surface of the cell approximately once every 10 min (ref. 2). In my experiments, such a rate should have led to a rapid decrease in the intensity of labelling with increasing periods of locomotion. I have not estimated fluorescence quantitatively, but qualitatively no such decrease was observed. Cells that had been allowed to move for periods of up to 180 min were apparently as fluorescent as control cells that had not moved and it was still possible to label fluorescently cells that had been maintained at 37 °C for 24 h after incubation with anti-Thy-1.1.

In considering the dilution of the cell-surface label in this way I make two assumptions. First, if the membrane is disassembled, Thy-1.1/anti-Thy-1.1 complexes will be degraded and cannot be reintroduced into the membrane for subsequent re-labelling. Second, at the proposed membrane sink, anti-Thy-1.1 is not released from the Thy-1.1 antigen and is therefore not available to diffuse through the medium to bind to uncomplexed Thy-1.1 antigen.

Both assumptions seem justified, as membrane-bound antibodies are usually endocytosed, enter the lysosomal system and are degraded^{13,14}. Membrane-bound cationised ferritin has been reported to enter secretion granules and Golgi cisternae¹⁵, but even there it had often lost its association with the membrane¹⁵. Even if the second assumption was incorrect and anti-Thy-1.1 was released at the sink, its recomplexing with unoccupied Thy-1.1 would have to be unexpectedly efficient to have maintained the observed levels of fluorescence, in view of the predicted rates of membrane assembly and disassembly and its likely rate of diffusion in the culture medium.

It seems unlikely from the results presented here that cell locomotion involves the assembly and disassembly of membrane components at the rate predicted by the membrane flow model.

Probably the backward movement of Con A receptors, and possibly also that of particles, during locomotion, results from a ligand-induced redistribution of membrane components. However, it is difficult to account for the commonly observed¹⁶ backward movement of blebs and ruffles in this way. The movement of these membranous organelles suggests that some backwardly directed force is generated on the surface of moving cells, but it seems unlikely to be due to the flow of intact membrane. Conceivably, the proposed flow of the membrane lipids alone¹⁷ could generate such a force, but this flow remains to be demonstrated.

I thank Dr P. Lake for the anti-Thy-1.1 antiserum and Dr Joan Heaysman and Professor Martin Raff for helpful comments and advice.

Received 15 June; accepted 30 August 1979.

1. Abercrombie, M., Heaysman, J. E. M. & Pegrum, S. M. *Expt Cell Res.* **62**, 389–398 (1970).
2. Harris, A. K. & Dunn, G. A. *Expt Cell Res.* **73**, 519–523 (1972).
3. Abercrombie, M., Heaysman, J. E. M. & Pegrum, S. M. *Expt Cell Res.* **73**, 536–539 (1972).
4. Harris, A. K. *Nature* **263**, 781–783 (1976).
5. Nicolson, G. L. *Int. Rev. Cyt.* **39**, 89–190 (1974).
6. Nicolson, G. L., Poste, G. & Ji, T. H. in *Dynamic Aspects of Cell Surface Organisation* (eds Poste, G. & Nicolson, G. L.) 1–73 (North-Holland, Amsterdam, 1977).
7. de Petris, S. & Raff, M. C. *Ciba Fdn Symp.* **14**, 27–41 (1973).
8. Vasiliev, J. M., Gelfand, I. M., Domnina, L. V., Dorfman, N. A. & Pletynshkina, O. Y. *Proc. natn. Acad. Sci. U.S.A.* **73**, 4085–4089 (1976).
9. Reif, A. E. & Allen, J. M. V. *J. exp. Med.* **120**, 413–433 (1964).
10. Stern, P. L. *Nature new Biol.* **246**, 76–78 (1973).
11. Brookes, J. P., Fields, K. L. & Raff, M. C. *Nature* **266**, 364–366 (1977).
12. de Petris, S. & Raff, M. C. *Eur. J. Immun.* **4**, 130–137 (1974).
13. Engers, H. D. & Unanue, E. R. *J. Immun.* **110**, 465–475 (1973).
14. Knopf, P. M., Destree, A. & Hyman, R. *Eur. J. Immun.* **3**, 251–259 (1973).
15. Farquhar, M. G. *J. Cell Biol.* **77**, R35–R42 (1978).
16. Harris, A. K. *Ciba Fdn Symp.* **14**, 3–20 (1973).
17. Bretscher, M. S. *Nature* **260**, 21–23 (1976).
18. Raff, M. C. *Nature* **244**, 378–379 (1969).

Five kinds of patterns were found using samples from randomly selected caucasians, as shown in Fig. 1: (1) F=S, (2) S only, (3) F only, (4) F>S, (5) F<S. When the stained crossed immunoelectrophoresis patterns were subjected to quantification of the ratio between the F and S peaks by placing the patterns over 1-mm graph paper and counting squares, for F>S, F/S was $219 \pm 25\%$ (± 1 s.d.) for $n = 10$ and for F<S, F/S was $52 \pm 7\%$ for $n = 10$. For F=S, the ratio was $96 \pm 8\%$, with $n = 13$. Thus, patterns (2) and (3) are, as described by O'Neill and coworkers¹⁵, from individuals who are $C4 f^0 S/f^0 S$ and $C4 F^0 S/F^0 S$, respectively, and patterns (4) and (5) are from individuals predicted by them to occur but not distinguishable by their typing system, $C4 F^0 S/FS$ and $C4 f^0 S/FS$. Pattern (1) is the only ambiguous phenotype, as it would be given by both $C4 FS/FS$ and $C4 f^0 S/f^0 S$ individuals.

The concentrations^{18,19} of C4 in the plasma (as per cent normal) of various C4 types are: for 32 FS/FS individuals, $109 \pm 44\%$ (± 1 s.d.); for 24 $F^0 S/FS$ individuals, $101 \pm 48\%$; for 9 $F^0 S/f^0 S$ individuals, $75 \pm 24\%$; for 18 $FS/f^0 S$ individuals, $100 \pm 56\%$; for 4 $f^0 S/f^0 S$ individuals, $70 \pm 24\%$; and for 7 $F^0 S/f^0 S$ individuals, $67 \pm 24\%$. It is of interest that the means of C4 serum concentration in individuals of different C4 types differed, as expected. However, there was considerable overlap,

Genetic polymorphism of human complement C4 and detection of heterozygotes

Z. L. Awdeh, D. Raum & C. A. Alper

Center for Blood Research, Boston, Massachusetts 02115

Many components of complement exhibit inherited structural polymorphism, with at least two alleles being common in one or more of the major races of man^{1–9}. However, definition of genetic polymorphism in human C4 has proved a difficult task. Differences between the electrophoretic patterns of C4 in EDTA plasma from different individuals were detected by Rosenfeld and coworkers^{10,11}, but these differences could not be explained by any simple genetic model. O'Neill and coworkers¹², using a system similar to that of a previous study¹³, interpreted the electrophoretic patterns in a completely different way from previous workers^{13,14}, stating that there were three: F, FS and S. They also found that C4 F carried Rodgers or Rg(a+) serologic reactivity and C4 S carried Chido or Ch(a+) reactivity¹⁵. These 'blood group' antigens had previously been shown to be closely linked to HLA^{16,17}. O'Neill proposed¹⁵ that C4 is genetically controlled by two closely linked loci, one for C4 F and one for C4 S, and postulated that deficiency states for one or the other locus are common but rarely occur together. The sets of haplotypes were postulated to be $C4 F^0 S$ (or $C4 F$), $C4 f^0 S$ (or $C4 S$) and $C4 FS$. In this model, the C4 F individuals are Rg(a+)Ch(a-), C4 S individuals are Rg(a-)Ch(a+) and C4 FS persons are Rg(a+)Ch(a+). The chief problem with the methods of typing, both electrophoretic and serologic, is that $C4 F^0 S$ and $C4 f^0 S$ can usually only be detected in the homozygous state, thus severely limiting their usefulness. We have now developed a method of C4 typing that allows detection of $C4 F^0 S$ and $C4 f^0 S$ in heterozygotes, and permits the study of genetic polymorphism of C4 in the general population. Our observations confirm and extend the two-locus genetic model of O'Neill and coworkers.

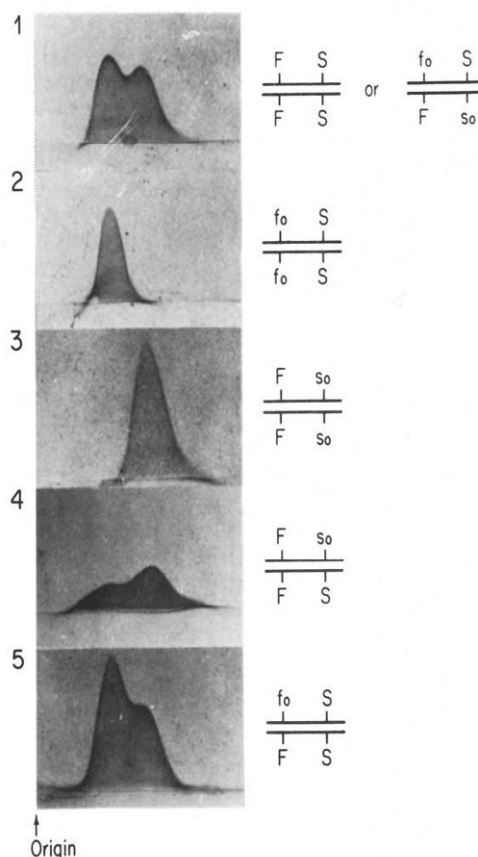


Fig. 1 Crossed immunoelectrophoresis patterns for the five detected phenotypes of C4. Fresh plasma from whole blood collected into Na₂ EDTA at 1.1 mg ml⁻¹ was used immediately or stored at -80 °C and thawed just before analysis. The plasma samples were incubated with neuraminidase (Sigma) from *Clostridium perfringens* at 5 U ml⁻¹ for 15 h at room temperature while dialysed against 0.1 M phosphate buffer, pH 7.0, containing 0.005 M Na₂EDTA. Desialated plasma samples were then subjected to electrophoresis in 0.8% agarose (Marine Colloids) using 0.075 M Veronal buffer containing 0.005 M EDTA at pH 8.6 for both gel and vessels. Electrophoresis was carried out at 300 V and 50 mA for 3 h by which time a HbA marker had migrated 6.0 cm. Gel strips (3 mm wide) containing separated proteins and extending from the origin to the HbA area were transferred to a second agarose gel containing goat anti-human C4 (Atlantic Antibodies) at 1% and then subjected to crossed immunoelectrophoresis²⁵. In a few instances, immunofixation²⁶ with anti-C4 was used after the first separation.

so that serum C4 concentrations were of little use in distinguishing C4 types, including C4FS/FS from C4f⁰S/FS⁰, or even C4FS⁰/FS⁰ and C4f⁰S/f⁰S from C4FS/FS.

When the frequencies of haplotypes FS, f⁰S and FS⁰ were calculated in a population of 203 randomly selected caucasians assuming all F=S patterns to be of genotype FS/FS, the frequencies of FS, FS⁰ and f⁰S were, respectively, 0.74, 0.14 and 0.12. These frequencies were not significantly different from those predicted by the Hardy-Weinberg equilibrium ($P = 0.54$). The frequency of FS is overestimated (by about 3%) and the frequencies of f⁰S and FS⁰ are underestimated. Evidence for the autosomal codominant inheritance of these C4 genes was obtained in family studies, as shown in Table 1 in which only expected types were found in offspring of various mating pairs, and the offspring types and ratios were close to those predicted. Inheritance of C4 haplotypes for three families is illustrated in Fig. 2.

Although the genetic model for C4 polymorphism in man as suggested by O'Neill and coworkers¹⁵ explains some of the previously confusing and conflicting observations, the problem of detecting the various proposed C4 'haplotypes' in their heterozygous combinations remained. In our experiments, overlap between C4 F and C4 S occurred in all existing separation systems, including isoelectric focusing in polyacrylamide gel. O'Neill and Dupont²⁰ attempted to identify C4FS/f⁰S and C4FS/FS⁰ patterns based on the intensity of immunofixation bands in their system. By comparison with frequencies predicted by the Hardy-Weinberg equilibrium and their observed homozygote frequencies, they were able to detect less than 20% of predicted heterozygotes. For these reasons we used neuraminidase treatment to reduce heterogeneity of each of the two C4 locus products. This resulted in the ability to separate and quantify C4 F and C4 S by ordinary agarose gel electrophoresis, thereby permitting C4 genotypes to be determined in random individuals and families. Thus, it has become feasible to demonstrate the inheritance of C4 polymorphism by classic mendelian genetics.

The only remaining ambiguity in determining C4 haplotypes is the distinction between C4FS/FS and C4f⁰S/FS⁰ (F=S), much like AA and AO blood group genotypes manifested by the single phenotype, group A. This ambiguity could usually be resolved by family studies (see family I, Fig. 2). Homozygous C4

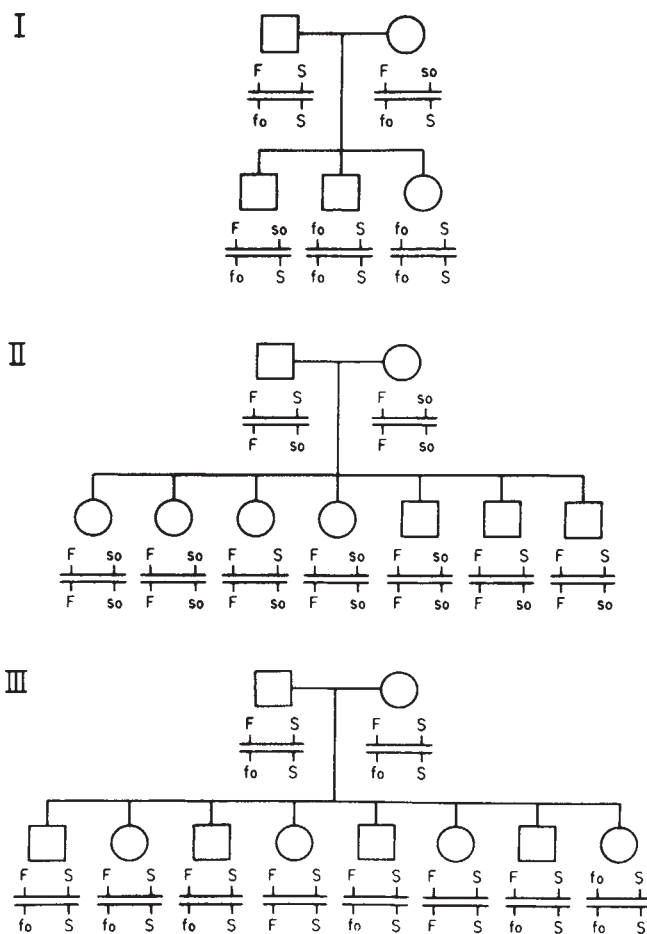


Fig. 2 Inheritance of C4 haplotypes in three families.

Table 1 Segregation of C4 types in families*

Mating	No. of matings	No. of offspring	Phenotypes of children					
			FS/FS	FS/f ⁰ S	FS/FS ⁰	FS ⁰ /FS ⁰	f ⁰ S/f ⁰ S	FS ⁰ /f ⁰ S
FS/FS × FS/FS	3	12	12					
			(12)					
FS/FS × FS ⁰ /FS ⁰	5	15	8		7			
			(7.5)		(7.5)			
FS/FS × f ⁰ S/f ⁰ S	3	9	3	6				
			(4.5)	(4.5)				
FS/FS × f ⁰ S/f ⁰ S	1	8	2	5			1	
			(2)	(4)			(2)	
FS/FS × FS ⁰ /FS ⁰	1	5	4		0	1		
			(1.25)		(2.5)	(1.25)		
FS/FS × f ⁰ S/f ⁰ S	1	4	0	1	2			1
			(1)	(1)	(1)			(1)
FS/FS ⁰ × FS ⁰ /FS ⁰	2	10			5	5		
					(5)	(5)		
FS/FS ⁰ × f ⁰ S/f ⁰ S	1	4					2	2
							(2)	(2)
FS/FS ⁰ × FS ⁰ /FS ⁰	1	5			2			3
					(2.5)			(2.5)

* By χ^2 analysis, expected (given in parentheses) and observed types in children did not differ significantly.

deficiency^{21,22} has been found in only six individuals and is thus extremely rare. There may also be ambiguity in the instance where the rare, presumed haplotype for this deficiency, C4f⁰S⁰, occurs in an individual with a single expressed structural haplotype. This problem, of course, is found in any genetically polymorphic system where a silent gene or haplotype is present. In this case, it is possible that 'anomalous' inheritance of structural types occurs.

In the mouse, a duplication of the C4 locus, Ss and Slp, within the H-2 region, also seems to occur, although one of these proteins, Slp, is not functional²³. In the guinea pig, only one genetic locus has been detected for C4 (ref. 24). In man, C4 patterns are due to the products of two loci in which the two genes are probably so closely linked that crossing over between them is an unusual event. This and the ability to detect heterozygotes of all possible haplotypes will eventually allow proper segregation and linkage analysis for C4 especially with regard to the genetic loci for the complement proteins, C2 and Bf, and the HLA complex.

This work was supported by grants AI 14157, AI 15033, AM 16392 and AI 13626 from the NIH.

Received 29 May; accepted 12 September 1979.

- Alper, C. A. & Rosen, F. S. in *Advances in Human Genetics* Vol. 7 (eds Harris, H. & Hirschhorn, K.) 141-188 (Plenum, New York, 1976).
- Alper, C. A. & Propp, R. P. *J. clin. Invest.* **47**, 2181-2191 (1968).
- Azen, E. A. & Smithies, O. *Science* **162**, 905-907 (1968).
- Alper, C. A., Boenisch, T. & Watson, L. *J. exp. Med.* **135**, 68-80 (1972).
- Hobart, M. J., Lachmann, P. J. & Alper, C. A. in *Protides of the Biological Fluids* Vol. 22, (ed. Peeters, H.), 575-580 (Pergamon, New York, 1975).
- Raum, D. et al. *J. clin. Invest.* **64**, 858-865 (1979).
- Alper, C. A. *J. exp. Med.* **144**, 1111-1115 (1976).
- Hobart, M. J. & Lachmann, P. J. *Transplant Rev.* **32**, 26-42 (1976).
- Hobart, M. J., Joysey, V. & Lachmann, P. J. *Immunogenet.* **5**, 157-163 (1978).
- Rosenfeld, S. I., Ruddy, S. & Austen, K. F. *J. clin. Invest.* **48**, 2283-2292 (1969).
- Bach, S., Ruddy, S., MacLaren, J. A. & Austen, K. F. *Immunology* **21**, 869-878 (1971).

12. O'Neill, G. J., Yang, S. Y., Tegoli, J., Berger, R. & Dupont, B. *Nature* **273**, 668–670 (1978).
13. Mauff, G., Bender, K. & Fischer, B. *Vox Sang.* **34**, 296–301 (1978).
14. Teisberg, P., Åkesson, I., Olaisen, B., Gedde-Dahl, T. Jr & Thorsby, E. *Nature* **264**, 253–254 (1976).
15. O'Neill, G. J., Yang, S. Y. & Dupont, B. *Proc. natn. Acad. Sci. U.S.A.* **75**, 5165–5169 (1978).
16. Middleton, J. *et al.* *Tissue Antigens* **4**, 366–373 (1974).
17. Giles, C. M. *et al.* *Tissue Antigens* **8**, 143–149 (1976).
18. Laurell, C.-B. *Analyt. Biochem.* **15**, 45–52 (1966).
19. Ritchie, R. F., Alper, C. A., Graves, J., Pearson, N. & Larson, C. *Am. J. clin. Path.* **59**, 151–159 (1973).
20. O'Neill, G. J. & Dupont, B. *Transplant Proc.* **11**, 1102–1106 (1979).
21. Hauptmann, G., Grosshans, E. & Heid, E. *Ann. Dermatol. Syphiligr. (Paris)* **101**, 479–496 (1974).
22. Ochs, H. D. *et al.* *New Engl. J. Med.* **296**, 470–475 (1977).
23. Ferreira, A., Nussenzweig, V. & Gigli, I. *J. exp. Med.* **148**, 1186–1197 (1978).
24. Bitter-Suermann, D., Krönke, M., Brade, V. & Hadding, U. *J. Immun.* **118**, 1822–1826 (1977).
25. Laurell, C.-B. *Analyt. Biochem.* **10**, 358–361 (1965).
26. Alper, C. A. & Johnson, A. M. *Vox Sang.* **17**, 445–452 (1969).

Genetic defect in secretion of complement C5 in mice

Yuet M. Ooi & Harvey R. Colten

Division of Cell Biology (Cystic Fibrosis), Department of Medicine, Children's Hospital Medical Center, and Department of Pediatrics, Harvard Medical School, Boston, Massachusetts 02115

A genetic deficiency of the fifth (C5) component of complement^{1–3}, a serum glycoprotein of molecular weight (MW) 220,000 (ref. 4), has been found in 39% of inbred strains of mice³. Sera of deficient mice lack detectable C5 activity and protein^{2,3}. In addition deficient mice produce antibody to mouse C5 when injected with sera from C5 sufficient (normal) strains. Levy *et al.*⁵ showed that somatic cell hybrids between C5 deficient (B10.D2/old line) macrophages and either C5 sufficient (B10.D2/new line) mouse kidney or chicken erythroblasts secreted haemolytically active mouse C5 *in vitro*. Several possible molecular mechanisms to account for the findings were considered, but insufficient direct data were available to choose among them. We recently reported that mouse (CD.1 strain) peritoneal cells in culture synthesise and secrete a single chain precursor, pro-C5 (MW ~ 210,000), of the two-chain (α chain, 125,000 and β chain 83,000 MW) C5 protein⁶. Radiolabelled precursor C5 was contained within the cells and was secreted into the tissue culture media. Using similar methods, we now find that C5 deficiency in each of five different mouse strains (AKR, SWR, DBA/2J, A/HeJ and B10.D2/old line) is due to a failure in secretion of C5 protein and not to a failure in biosynthesis of pro-C5.

Resident peritoneal macrophage cultures from five mouse strains genetically C5 deficient and from two normal (Swiss and B10.D2/new line) strains were established and pulsed with medium containing ³⁵S-labelled methionine. After 24 h, newly synthesised intracellular (cell lysate) and extracellular protein were quantitated by trichloroacetic acid (TCA) precipitation, specific C5 antigen by immunoprecipitation and C5 function in the extracellular medium by haemolytic assay. The size and subunit composition of the radiolabelled C5 protein were determined on SDS-polyacrylamide gel electrophoresis in reducing conditions.

Total protein (TCA-precipitable radioactivity) was similar in C5-deficient and normal cells in both the intracellular and extracellular compartments (Table 1). ³⁵S-methionine was incorporated into C5 antigen contained intracellularly and was secreted by normal peritoneal cell cultures. Although peritoneal cells from the deficient strains synthesised an amount of immunochemically detectable C5 protein similar to that produced by the normal strains, all of the C5 antigen was contained in the cell lysates (Table 1). In addition, approximately 2.5×10^8 haemolytically active C5 molecules ml⁻¹ were

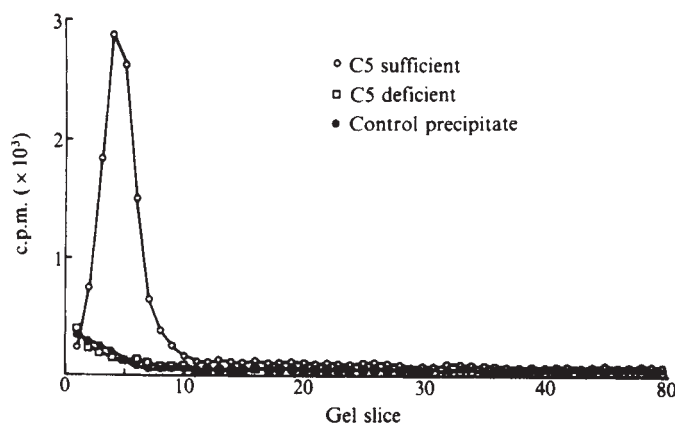


Fig. 1 SDS-polyacrylamide gel electrophoresis of reduced and alkylated C5 protein secreted by mouse peritoneal macrophages from Swiss (C5 sufficient) and A/HeJ (C5 deficient) strains. Confluent resident peritoneal cell cultures were established by placing 12×10^6 cells suspended in Dulbecco's modified Eagle's medium (DMEM) with 20% heated fetal calf serum in 60 mm Falcon plastic dishes. After incubating the cells at 37 °C for 1 h in humidified 5% CO₂:95% air to permit adherence, the dishes were washed with DMEM, then fed with DMEM (lacking unlabelled methionine), containing ³⁵S-methionine (80 μ Ci ml⁻¹), 50 mM ϵ -aminocaproic acid, 0.2% lactalbumin, 100 U ml⁻¹ penicillin and 100 μ g ml⁻¹ streptomycin. The medium was removed 24 h later, fresh medium containing ³⁵S-methionine was added, and the cultures were incubated for a further 24 h. Medium was collected and centrifuged at 10,000g for 10 min to remove floating cells and debris. The cell monolayer was washed three times in phosphate-buffered saline, then lysed in Tris-KCl with 0.01 M Na EDTA, 0.1 M ϵ -aminocaproic acid, and 0.5% deoxycholate, and 0.5% Triton X-100 buffer⁶, then centrifuged at 10,000g for 45 min. Total labelled protein was assessed by TCA precipitation of 5- μ l aliquots (Table 1). Antiserum to mouse C5 was produced in C5 deficient (B10.D2/old line) mice by immunisation with normal (B10.D2/new line) mouse serum in complete Freund's adjuvant^{2,6}. Specific C5 and control (ovalbumin) immunoprecipitates were formed as previously described^{6,7}, using unlabelled carrier proteins and antisera sufficient to yield 30 μ g protein in the precipitates. They were washed, dried and then dissolved by boiling for 2 min in 40 μ l buffer consisting of 10 mM Tris, 1 mM EDTA, 1% SDS, 4% 2-mercaptoethanol, 10% glycerol and Pyronine Y. Iodoacetamide (60 mM final concentration) was added and the mixtures incubated at 37 °C for 30 min. Aliquots of 5 μ l were removed for estimates of specific incorporation of labelled methionine into C5 antigen (Table 1) and the remainder was applied to 5.6% polyacrylamide, 1% SDS disc gels. Electrophoresis, slicing and counting of samples and analysis of standard gels were performed as previously described^{6,7}. Radioactivity in C5 antigen from C5-sufficient (Swiss) cell culture medium (○), C5-deficient (A/HeJ) cell culture medium (□) and control immunoprecipitates (●) are plotted. Peak of radioactivity (○) corresponds to estimated MW of 220,000.

present in the normal peritoneal cell culture media, but none was detected in any of the deficient cell culture media (limits of detection <2% of normal).

Analysis of the C5 protein produced by normal cells on SDS-polyacrylamide gel electrophoresis showed a single peak of radioactivity (mobility corresponding to MW 220,000) in the extracellular medium (open circle, Fig. 1) and two peaks (MW 201,000 and 34,000) in the cell lysate (open circle, Fig. 2), in agreement with previous findings⁶. Radioactivity in control immunoprecipitates (ovalbumin/anti-ovalbumin) distributed uniformly throughout the gels without recognisable peaks (closed circles). No peak of immunoprecipitable C5 radioactivity was detected extracellularly (open squares, Fig. 1) in any of the C5-deficient cell cultures, but a pattern comparable to the normal was observed in the intracellular compartment (MW 200,000 and 38,000 peaks) (open squares, Fig. 2). Figures 1 and 2 show the result with A/HeJ cells; similar patterns were seen on analysis of the other deficient cell culture media and lysates. Following a 24-h pulse with labelled methionine, a 48-h

Table 1 Synthesis and secretion of C5 and total protein by mouse peritoneal macrophages

C5 antigen						
Strain	Serum	Extracellular (c.p.m.)	Intracellular (c.p.m.)		Total protein c.p.m. ($\times 10^{-3}$)	
			High MW	Low MW	Extracellular	Intracellular
A/HeJ	—	—115	970	2,700	3.5	74.9
AKR	—	50	1,600	2,960	5.1	100
B10.D2/old	—	—5	2,080	4,220	8.2	101
DBA/2J	—	—170	3,430	5,730	12.8	129
SWR	—	80	3,600	7,900	8.9	168
Swiss	+	1,820	2,030	3,380	8.2	100

Sera from mice used for peritoneal macrophage cultures were tested for the presence of C5 antigen by Ouchterlony analysis (results in agreement with findings in ref. 3). Peritoneal cell cultures were established as described in Fig. 1 legend and the extracellular C5 antigen estimated in 125- μ l aliquots by subtracting the radioactivity in control (ovalbumin/anti-ovalbumin) immunoprecipitates (mean 427 c.p.m. per 125 μ l; range 523 for B10.D2/old line to 308 for AKR) from radioactivity in C5-anti-C5 immunoprecipitates. Intracellular C5 antigen content was estimated from the radioactivity in the high MW pro-C5 peak and low MW peak on SDS-polyacrylamide gel electrophoresis of C5 immunoprecipitates (representative pattern is shown in Fig. 2). To estimate total protein synthesis, TCA precipitation was performed on 5- μ l aliquots as described in Fig. 1 legend.

chase of C5-deficient (A/HeJ) cells with medium containing unlabelled methionine resulted in little change in the intracellular C5 antigen pattern on SDS-polyacrylamide gel electrophoresis and no appearance of labelled C5 protein in the extracellular medium. Estimation of pool size and intracellular turnover of C5 antigen cannot be determined, but within the time limits of the experiments, even delayed secretion of labelled C5 antigen was ruled out.

The possibility was considered that macrophages from the deficient strains secreted an unstable C5 precursor protein or a proteolytic enzyme that destroyed normal pro-C5. Accordingly, intracellular C5 protein produced by and prepared from A/HeJ (C5-deficient) cells was incubated for 30 min at 37°C with unlabelled, C5-deficient (A/HeJ) conditioned medium, C5-sufficient (Swiss) conditioned medium or fresh medium alone. No degradation of labelled pro-C5 (MW ~ 200,000) or the small MW (38,000) proteins was observed on SDS-polyacrylamide gel electrophoresis of the incubation mixtures.

These data suggest that C5 deficiency in mice is due to a defect in secretion. This may result from a failure of glycosylation as has been proposed as a mechanism for a defect of secretion in certain human immunoglobulin deficiency diseases⁸, a mutant mouse myeloma⁹ and in normal plasma cells exposed to tunicamycin¹⁰. A missense mutation could lead to a lack of a suitable site for glycosylation on the C5 polypeptide chain. Alternatively, the defect might reside in synthesis of a protein required specifically for C5 glycosylation or for C5 secretion. In any case, these experiments indicate that the C5 mRNA is translated in cells from several mouse strains genetically deficient in C5, but that the product (pro-C5) is not secreted.

Received 6 August; accepted 5 September 1979.

1. Rosenberg, L. T. & Tachibana, D. K. *J. Immun.* **89**, 861–867 (1962).
2. Cinader, B. & Dubiski, S. *Nature* **202**, 102–103 (1964).
3. Cinader, B., Dubiski, S. & Wardlaw, A. C. *J. exp. Med.* **120**, 897–924 (1964).
4. Nilsson, U. R., Mandle, R. J. & McConnell-Mapes, J. A. *J. Immun.* **114**, 815–822 (1975).
5. Levy, N. L. *et al. Proc. natn. Acad. Sci. U.S.A.* **70**, 3125–3129 (1973).
6. Ooi, Y. M. & Colten, H. R. *J. Immun.* (in the press).
7. Hall, R. E. & Colten, H. R. *Proc. natn. Acad. Sci. U.S.A.* **74**, 1707–1710 (1977).
8. Cicciama, F. *et al. J. clin. Invest.* **57**, 1386–1390 (1976).
9. Weitzman, S. & Scharff, M. D. *J. molec. Biol.* **102**, 237–252 (1976).
10. Hickman, S. A. *et al. J. biol. Chem.* **252**, 4402–4408 (1977).

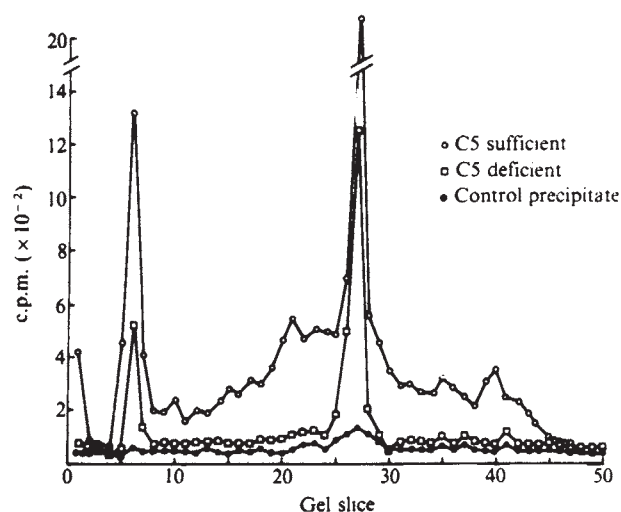


Fig. 2 SDS-polyacrylamide gel electrophoresis of radiolabelled reduced and alkylated C5 protein contained in cell lysates of mouse peritoneal cells from Swiss (C5-sufficient, ○), and A/HeJ (C5-deficient, □) strains. Radioactivity in control immunoprecipitates indicated by closed circles. Estimated MW of the large MW peak was 203,000. In other experiments, estimates ranged from 201,000 to 210,000. The low MW peak was 34,000–38,000. This low MW peak does not correspond in size to a known subunit of C5. A similar pattern of intracellular labelled C5 antigen (two peaks—205,000 and 38,000 MW) was observed in a detergent lysate of Swiss mouse spleen cells obtained from an animal injected with 5 mCi ³⁵S-methionine (supplied by Dr Allen Schwartz).

Bombesin suppresses feeding in rats

J. Gibbs & D. J. Fauser

Department of Psychiatry, Cornell University Medical College, Bourne Laboratory, The New York Hospital, White Plains, New York 10605

E. A. Rowe, B. J. Rolls, E. T. Rolls & S. P. Maddison

Department of Experimental Psychology, University of Oxford, Oxford, UK

Bombesin (BBS) is a tetradecapeptide originally isolated from amphibian skin¹. BBS-like immunoactivity is widely distributed in mammalian gut^{2–5}, and plasma levels have been shown to rise sharply following feeding (ref. 6 and V. Erspamer, personal communication). The physiological actions of BBS are unknown. We have previously shown that the classic gut hormone cholecystikinin (CCK) is a powerful and specific suppressor of food intake^{7–9}. Although CCK and BBS lack common amino acid sequences, they have certain common actions on gut viscera^{10,11}. We have now shown that BBS also suppresses food intake, and we compare its action with that of CCK.

Eleven male Sprague-Dawley rats weighing 440–520 g were housed and tested in individual cages on an artificial 12-h light cycle. They were maintained on solid food pellets (Purina) overnight and tested with a balanced liquid food preparation (No. 116EC, GIBCO) diluted 1:3 with deionised water. Solid food was removed at 0930 h each morning, and rats were then allowed access to liquid food for 30 min. This pre-deprivation meal of liquid food assured that all rats had eaten a meal shortly before they were deprived of all food at 1000 h. Immediately before the presentation of liquid food in graduated drinking tubes for the test at 1300 h, rats were injected intraperitoneally (i.p.) with 1 ml of one of the following treatments on different days: (1) synthetic BBS in doses of 2, 4, 6, 8, 16 μg per kg body weight, diluted in 0.15 M NaCl; (2) synthetic C-terminal octapeptide of CCK (CCK8) in doses of 0.2, 0.4, 0.7, 1.4, 2.9 μg per kg, diluted in 0.15 M NaCl; (3) equivolumetric controls of 0.15 M NaCl. Food intake was measured at 5 and 15 min, and then at 15-min intervals for the remainder of the 180-min test. The behaviour of each rat was noted¹² during a 4-s interval every minute for the first 45 min of the test. This systematic observation of the behaviours of each animal permitted calculations of the incidences and pattern of the behaviours associated with feeding (exploration, grooming, apparent sleep), so that control and peptide-injected rats could be quantitatively compared; it also permitted the identification of any abnormal behaviour. In all tests, each animal served as its own control; statistical comparisons were made with a matched-pair *t*-test.

BBS and CCK8 each produced a large suppression of liquid food intake across the entire range of doses tested (Fig. 1). The smallest doses of each peptide produced equivalent 15% suppressions: 2 μg per kg BBS reduced food intake from a control of 18.8 ml to 15.9 ml ($P < 0.01$); 0.2 μg (~4 Ivy units) per kg CCK8 reduced intake from 18.6 to 15.8 ml ($P < 0.01$). The largest doses of each peptide also produced similar suppressions: 16 μg per kg BBS reduced intake from 20.5 ml to 8.1 ml ($P < 0.001$); 2.9 μg (~63 Ivy units) per kg CCK8 reduced intake from 17.1 ml to 5.4 ml ($P < 0.001$). A comparison of relative effectiveness on a molar basis revealed that the dose of BBS required to suppress feeding by 50% was five times greater than the equipotent dose of CCK8 (Fig. 1).

In a parallel experiment, the effects of BBS and CCK8 were also tested in animals given solid food (Purina rat pellets) following a 7 h (0900–1600 h) food deprivation. Both peptides reduced solid food intake. In these conditions, the lowest dose of BBS, 3 μg per kg, suppressed feeding by 21% (control intake, 2.8 g; intake after BBS, 2.2 g; $P < 0.05$). The lowest dose of CCK8, 1.1 μg (~24 Ivy units) per kg suppressed feeding by 30% (from 2.7 g to 1.9 g; $P < 0.01$). The largest dose of BBS tested, 6 μg per kg, suppressed feeding by 50% (from 2.8 g to 1.4 g; $P < 0.01$). The largest dose of CCK8, 3.8 μg (~84 Ivy units) per kg, suppressed feeding by 77% (from 2.6 g to 0.6 g; $P < 0.001$).

The actions of BBS and CCK8 were similar in two respects. Both peptides suppressed feeding rapidly, with maximum reductions occurring during the first 15 min after injection. In addition, both peptides produced transient suppressive effects: even after large doses, cumulative food intakes of peptide-injected rats had returned to normal levels within 120 min. However, the actions of the two peptides differed in one respect. Although both suppressed liquid and solid food intakes, CCK8 was two to five times as potent in suppressing liquid food intake as it was in suppressing solid food intake, a differential we have noted previously⁷. In contrast, BBS suppressed solid and liquid food intakes equally. Thus, the potency of CCK8 varied according to the physical characteristics of the test diet, whereas the potency of BBS did not.

As BBS suppressed solid as well as liquid food intakes, the suppression was not achieved through some interference with the motor acts required for licking. Furthermore, the largest dose of BBS tested had no effect on water consumption after the minimal water deprivation (6 h) required to achieve reliable intakes. Thus, BBS preferentially reduced feeding, not drinking, even when the same motor act (licking metal spouts for liquid

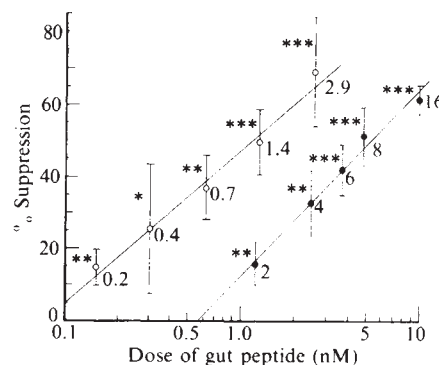


Fig. 1 Suppression of liquid food intake in rats ($n = 11$) during the first 15 min after i.p. injections of various doses of BBS (●) or CCK8 (○). The figure shows mean per cent suppressions and s.e.m. compared with intake on control tests. Doses of each peptide are in μg per kg. Doses of the two peptides on the abscissa are arranged along a molar logarithmic scale. Control intakes of liquid food ranged from 13.7 to 20.5 ml (mean 18.1 ml, s.e.m. 0.3 ml). * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, statistical differences from respective 0.15 M NaCl controls. Correlation coefficients (Pearson product-moment): for BBS, $r = 0.91$ ($P < 0.025$); for CCK8, $r = 0.97$ ($P < 0.005$). Slopes of the regression lines were not significantly different³¹ ($t = 0.22$, $P > 0.05$).

food or water) was required for either ingestive behaviour; this differential strongly suggests that BBS did not reduce feeding simply by producing some generalised discomfort. Several further observations also indicated that BBS did not cause illness or distress. First, the rats never seemed acutely or chronically ill, and they gained weight normally during 8 months of frequent testing. Second, after injections of BBS, rats always began eating eagerly; they merely stopped sooner. Thus, no statistically significant differences in food intake between BBS- and saline-injected rats occurred during the first 5 min of feeding, but BBS-injected rats ate much less than saline-injected rats between 5 and 15 min of the test. This ineffectiveness of BBS in preventing or slowing the early phase of feeding was not an artefact of the time required for the distribution of exogenously injected BBS as it occurred whether the peptide was injected immediately before, 5 min before, or 15 min before food presentation. Thus, BBS preferentially acted to enhance satiety by shortening the meal; it did not prevent or delay the onset of a meal, nor did it slow the initial phase of eating. Third, analysis of the minute-by-minute behavioural data revealed that the only significant behavioural change produced by BBS was a decrease in the incidence of feeding (Table 1).

These data demonstrate that BBS did not reduce food intake simply by causing a generalised disruption of behaviour; rather, it produced a selective suppression of feeding, a quality which one would anticipate in a natural satiety signal. Furthermore, in no instance did BBS elicit any abnormal behaviour. Finally, in our unpublished observations, doses of BBS as high as 128 μg per kg have failed to produce any evidence of illness or distress in similar test conditions. Although intracisternal BBS can reduce core body temperature of cold-exposed rats¹³, we found no change in core body temperature, as measured by rectal thermoprobe, 15 or 30 min after i.p. injections of doses of 4–32 μg per kg, the times when suppression of feeding was maximal.

The mediation of the satiety action of BBS is unknown. The slopes of the regression lines drawn for the BBS and CCK8 dose-response curves were not significantly different statistically (see Fig. 1). Parallelism of curves is consistent with but not proof of the same mechanism of action¹⁴. This parallelism might be explained if exogenous BBS produces its satiety effect simply by releasing endogenous CCK^{10,15–17}. However, as described above, comparison of the dose-response curves for liquid and solid foods revealed a situation in which the effects of BBS and CCK8 diverged, depending on the physical characteristics of food ingested; this divergence demonstrates that the satiety

Table 1 Incidence of behaviours occurring after i.p. injection of BBS (8 µg per kg) or vehicle control (0.15 M NaCl) in 11 rats

	Feeding	Exploration, grooming	Apparent sleep	Miscellaneous
Control	15	19	65	1
BBS	5*	23	71	1

Incidences are expressed as mean % of the total number of behavioural observations carried out. During the first 45 min of the test the only statistically significant effect which BBS produced was a reduction in the incidence of feeding.

* $P < 0.001$, BBS compared with control. All other BBS-control comparisons were nonsignificant ($P > 0.4$).

action of exogenous BBS cannot be mediated solely by endogenous CCK. Three observations of visceral gut actions of BBS relate to this point. (1) In humans, Basso *et al.*¹¹ have shown that the addition of secretin to a slow intravenous infusion of BBS caused a partial inhibition, rather than a potentiation, of BBS-induced pancreatic amylase output, suggesting that secondarily released CCK is not the major mediator of BBS-induced amylase output in these conditions. (2) Although enterectomy abolishes BBS-induced pancreatic protein secretion in the dog¹⁵ it does not affect this action in the rat¹⁸. (3) BBS powerfully stimulates amylase release from *in vitro* preparations of rat pancreatic fragments^{19,20} or dispersed acinar cells²¹. These findings strongly suggest that BBS can directly stimulate traditional CCK target tissues.

We conclude that BBS is a putative satiety signal. The existence of at least one unidentified gastric satiety signal has recently been demonstrated in the rat^{22,23}. We have shown that the action of this gastric signal does not depend on vagal innervation²⁴, and may therefore be hormonal in nature. As it is present in large quantities in gastric mucosa⁴, BBS is a candidate for this unidentified satiety signal.

We have not determined how the amount of BBS required to elicit satiety in this study relates to the amount and pattern of BBS released by a normal meal, nor how BBS may interact with other putative satiety signals, such as CCK. Finally, the site of action of BBS when it alters satiety behaviour is unknown, but it is of interest that BBS immunoactivity^{4,5,25}, like that of CCK²⁶⁻³⁰, is present in large quantities in the brain.

We thank F. Gutman for assistance and J. D. Falasco, C. F. Martin, H. Pringle, K. J. Simansky and G. P. Smith for critical readings of the manuscript. Synthetic BBS was from R. de Castiglione (Farmitalia) and CCK8 was from M. Ondetti (Squibb). The research was supported by the American Philosophical Society, the Royal Society of Medicine Foundation, the USPHS (NIAMDD and NIMH) and the MRC.

Received 1 August; accepted 12 September 1979.

- Erspamer, V. & Melchiorri, P. *Pure appl. Chem.* **35**, 463-494 (1973).
- Walsh, J. H. & Holmquist, A. L. *Gastroenterology* **70**, A-90/948 (1976).
- Polak, J. M., Bloom, S. R., Hobbs, S., Solcia, E. & Pearse, A. G. E. *Lancet* **i**, 1109-1110 (1976).
- Walsh, J. H. & Dockray, G. J. *Gastroenterology* **74**, 1108 (1978).
- Brown, M., Allen, R., Villarreal, J., Rivier, J. & Vale, W. *Life Sci.* **23**, 2721-2728 (1978).
- Erspamer, V. & Melchiorri, P. *J. Endocr.* **70**, 12P-13P (1976).
- Gibbs, J., Young, R. C. & Smith, G. P. *J. comp. Physiol. Psychol.* **84**, 488-495 (1973).
- Gibbs, J., Falasco, J. D. & McHugh, P. R. *Am. J. Physiol.* **230**, 15-18 (1976).
- Gibbs, J. & Smith, G. P. *Acta hepato-gastroenterol.* **25**, 413-416 (1978).
- Erspamer, V. & Melchiorri, P. in *Gastrointestinal Hormones* (ed. Thompson, J. C.) 575-589 (University of Texas Press, Austin, 1975).
- Basso, N. *et al. Gut* **16**, 994-998 (1975).
- Antin, J., Gibbs, J., Holt, J., Young, R. C. & Smith, G. P. *J. comp. Physiol. Psychol.* **89**, 784-790, 1975.
- Brown, M., Rivier, J. & Vale, W. *Science* **196**, 998-1000 (1977).
- Goldstein, A., Aronow, L. & Kalman, S. M. *Principles of Drug Action: The Basis of Pharmacology*, 79 (Harper and Row, New York, 1968).
- Konturek, S. J., Krol, R. & Tasler, J. *J. Physiol., Lond.* **257**, 663-672 (1976).
- Fender, H. R., Curtis, P. J., Rayford, P. L. & Thompson, J. C. *Surg. Forum* **37**, 414-416 (1976).
- Miyata, M., Guzman, S., Raymond, P. L. & Thompson, J. C. *Gastroenterology* **74**, 1137 (1978).
- Linari, G., Baldieri Linari, M., & Lutoslawska, G. *Rc. Gastroenterol.* **9**, 179-184 (1977).
- Deschodt-Lanckman, M., Robberecht, P., De Neef, P., Lammens, M. & Christophe, J. *J. clin. Invest.* **58**, 891-898 (1976).
- Iwatsuki, N. & Petersen, O. H. *J. clin. Invest.* **61**, 41-46 (1978).
- May, R. J., Conlon, T. P., Erspamer, V. & Gardner, J. D. *Am. J. Physiol.* **235**, E112-E118 (1978).
- Kraly, F. S. & Smith, G. P. *Physiol. Behav.* **21**, 405-408 (1978).

- Deutsch, J. A., Young, W. G. & Kalogeris, T. J. *Science* **201**, 165-167 (1978).
- Kraly, F. S. & Gibbs, J. *Abstr. Soc. Neurosci.* **4**, 176, (1978).
- Villarreal, J. A. & Brown, M. R. *Life Sci.* **23**, 2729-2734 (1978).
- Dockray, G. J. *Nature* **264**, 568-570 (1976).
- Straus, E., Muller, J. E., Choi, H. S., Paronetto, F. & Yalow, R. S. *Proc. natn. Acad. Sci. U.S.A.* **74**, 3033-3034 (1977).
- Muller, J. E., Straus, E. & Yalow, R. S. *Proc. natn. Acad. Sci. U.S.A.* **74**, 3035-3037 (1977).
- Rehfeld, J. J. *biol. Chem.* **253**, 4022-4030 (1978).
- Innis, R. B., Correa, F. M. A., Uhl, G. R., Schneider, B. & Snyder, S. H. *Proc. natn. Acad. Sci. U.S.A.* **76**, 521-525 (1979).
- Goldstein, A. *Biostatistics: An Introductory Text*, 144 (Macmillan, New York, 1964).

Human β -thromboglobulin inhibits PGI₂ production and binds to a specific site in bovine aortic endothelial cells

W. Hope*, T. J. Martin*, C. N. Chesterman† & F. J. Morgan‡

* University of Melbourne, Department of Medicine, Repatriation General Hospital, Heidelberg, Victoria, Australia 3081

† University of Melbourne, Department of Medicine, St Vincent's Hospital, Fitzroy, Victoria, Australia 3065

‡ St Vincent's School of Medical Research, Fitzroy, Victoria, Australia 3065

Blood platelets have a major role in haemostasis through their aggregation and adherence to the damaged vessel wall. During this process, platelet granular constituents are released. Although the functions of many of these release products are well known, biological functions of some well defined platelet specific proteins have not been determined. This category includes platelet factor 4 (PF4) and β -thromboglobulin (β TG), both small proteins of molecular weight 30,000-36,000 (refs 1, 2) which are stored in the α granule of the platelet and have not been detected in any other tissue. β TG is composed of four identical noncovalently bound subunits and its amino acid sequence is significantly homologous with that of PF4 (ref. 3). Although PF4 possesses a marked ability to neutralise heparin, no physiological or pathophysiological role has been attributed to either protein. The discovery of prostacyclin (PGI₂) has led to a reappraisal of the factors regulating haemostasis and especially of the role of the vascular endothelium in preventing platelet adherence and aggregation⁴⁻⁶. The initial action of PGI₂ on the platelet is to stimulate adenylate cyclase⁷⁻⁹, and it is the most potent inhibitor of platelet aggregation yet discovered. Also, cultures of arterial and venous endothelial cells have been found capable of producing PGI₂ (refs 10, 11). We now report results indicating that β TG reduces the production of PGI₂-like activity in cultured bovine endothelial cells, which are shown to possess a specific receptor for β TG. The characteristics of this receptor suggest that β TG may act locally at high concentrations to favour platelet aggregation by diminishing PGI₂ production.

Monolayer cultures of aortic endothelial cells were established from bovine aortas obtained from animals immediately after slaughter and processed within 1 h. Endothelial cells were prepared from the bovine aorta by collagenase digestion according to the method of Gimbrone *et al.*¹², and grown in plastic culture bottles in medium RPMI-1640 with 40% fetal calf serum. Small groups of cells became established, grew to near confluence within about 1 week and were subcultured by washing the monolayer surface with 0.02% EDTA followed by incubation in 0.025% trypsin-EDTA for 1-2 min. Complete culture medium (5 ml) was then added, and the cells were washed and resuspended in medium to be plated out in fresh vessels. All experiments were carried out on the first to the fourth subcultures. For studies of PGI₂ production, cells were suspended as in routine subculture, but were washed once more before resuspension in a buffered salt solution (BSS). Substances

to be tested were added to this cell suspension at the desired concentrations, and an aliquot of the endothelial cell suspension containing a known number of cells was tested for its ability to inhibit arachidonic acid-induced aggregation of human blood platelets. Preliminary experiments had shown that incubation of cells with indomethacin (14 μ M) or tranilcyproline (500 μ M) abolished the ability of endothelial cells to inhibit platelet aggregation. Furthermore, incubation of endothelial cell cultures with 3 H- or 14 C-labelled arachidonate, followed by extraction and this layer chromatography of acidified medium, showed that the major labelled prostanoid product was 6-keto-prostaglandin $F_{1\alpha}$, which is the stable degradation product of the labile PGI_2 . No significant PGE_2 was formed in these conditions of short incubations.

Following incubation with human β TG, significantly more endothelial cells are required for complete inhibition of aggregation than in control incubations (Table 1). PF_4 , PGE_2 , isoprenaline, serotonin and nicotine had no effect in this system. The effect of β TG on endothelial cells was seen at concentrations which are of the same order as those in serum or platelet-rich plasma (PRP) during collagen-induced platelet aggregation¹³. β TG (10 μ g ml^{-1}) had no direct effect on the threshold concentration of arachidonate required to induce aggregation, nor did it influence the ability of synthetic PGI_2 to inhibit arachidonate-induced aggregation. These findings indicate that β TG decreases the production of PGI_2 -like biological activity by endothelial cells.

Table 1 Effect of incubation with β TG and other substances on endothelial cell numbers required to inhibit platelet aggregation

Treatment	Concentration	Relative no. of endothelial cells to inhibit aggregation	
Control	—	1.00	(23)
β TG	1 μ g ml^{-1}	2.30 $\pm$ 0.93	(5) $P < 0.05$
	2 μ g ml^{-1}	2.02 $\pm$ 0.43	(5) $P < 0.005$
	5 μ g ml^{-1}	4.60 $\pm$ 0.57	(3) $P < 0.02$
PF_4	10 μ g ml^{-1}	1.0	(3)
PGE_2	10 ⁻⁶ M	1.0	(1)
Serotonin	5 $\times$ 10 ⁻⁵ M	1.0	(3)
Isoprenaline	10 ⁻⁶ M	1.16 $\pm$ 0.05	(3) NS
Nicotine	10 ⁻⁶ M	1.0	(4)

Results are from 23 individual experiments studying the effects of various agents on the number of endothelial cells required to inhibit arachidonate (AA)-induced aggregation of human blood platelets. Blood was drawn from normal volunteers into 3.8% sodium citrate (1:9 v:v). PRP was prepared by centrifugation at 200g for 10 min at room temperature. The threshold concentration of AA (Sigma) required to cause platelet aggregation was determined with 0.4 ml of PRP in a Payton dual-channel aggregometer; normal subjects with no recent aspirin ingestion required 0.4–1 mM AA. Endothelial cell suspensions were prepared by subculturing cells from the primary to the fourth subculture. After the standard subculturing procedure (see text) cells were washed once in phosphate-buffered saline (PBS) and resuspended in BSS of the following composition: Tris 15 mM, NaCl 120 mM, KCl 4 mM, $MgSO_4$ 1.6 mM, NaH_2PO_4 2 mM, $CaCl_2$ 1.2 mM, glucose 10 mM, human serum albumin 0.1%, at pH 7.4. Cells were counted in a haemocytometer, and suspended to concentrations of 1–5 $\times$ 10⁶ per ml. Duplicate incubations of cell suspensions (0.5 ml) were carried out in 10-ml plastic tubes in a shaking incubator at 37 °C. The various treatments were added in BSS, and after at least 15 min incubation, samples of the incubations were tested for their ability to inhibit AA-induced platelet aggregation. β TG was prepared^{1,2} from the platelet release products of platelet concentrates and PF_4 from the supernatant of outdated platelet concentrates, as previously described¹⁹. Aggregation inhibition by the incubated cells was tested as follows. To 0.4 ml PRP in an aggregometer tube was added 10 μ l of cell suspension or of a dilution made in BSS. Dilutions were made until the minimum amount required to inhibit platelet aggregation was determined, from which the number of cells required to inhibit aggregation was calculated. In each experiment the procedure was repeated for control and treated cells at least twice. Each experiment was completed within 2 h of subculture. In all reported experiments the cell numbers (control and treated) required to inhibit aggregation remained constant throughout the experiment. When this was not the case, experiments were discontinued. The numbers of cells (control incubations) required to abolish threshold AA-induced aggregation varied from 1 to 80 $\times$ 10³ among the 23 different experiments; in all except 4 experiments a single treatment was tested. Each treatment is expressed as the relative number of cells ($\pm$ s.d.) required to abolish AA-induced aggregation compared with the control experiment which is expressed as unity; the number of individual experiments is given in parentheses. Statistical analysis was carried out using a logarithmic transformation of the relative cell numbers (paired *t*-test). With PF_4 , PGE_2 , serotonin and nicotine, the effective dilution never differed from that of the control. NS, not significant.

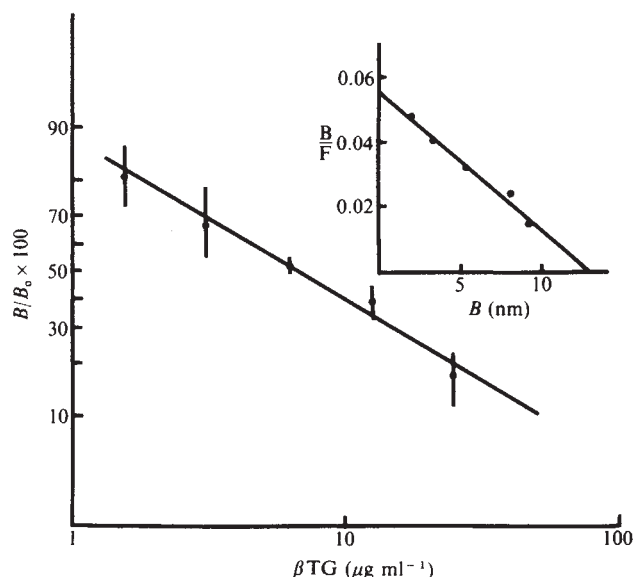


Fig. 1 Specific binding of 125 I- β TG to bovine aortic endothelial cells. Cells from the first subculture were dispersed (see text), washed twice with PBS and resuspended at a concentration of 5×10^6 cells ml^{-1} in BSS (see Table 1). Binding experiments were carried out for 1 h at 25 °C in 10-ml plastic tubes with vigorous shaking. Incubations in duplicate consisted of 0.3 ml of cell suspension and 0.2 ml BSS containing 125 I- β TG (55,000 c.p.m. per tube) and increasing amounts of unlabelled β TG or other substances to be tested. β TG was labelled with 125 I using the lactoperoxidase method as described previously²⁰; specific activity in this experiment was 200 μ Ci per μ g, and varied down to 50 μ Ci per μ g in other experiments. At 1 h 200- μ l duplicate samples were removed from the incubation, and centrifuged (Beckman Microfuge, Model B, 5 min, 10,000g). The supernatants were removed, the tips of the tubes containing the cell pellet cut off and the bound radioactivity estimated in a Packard spectrometer with 75% efficiency for counting 125 I. Nonspecific binding (NSB) was measured as radioactivity bound in the presence of excess β TG (50 μ g ml^{-1}) and was subtracted from the total radioactivity bound to obtain specific binding. Specific binding of 125 I- β TG in the absence of unlabelled β TG (B_0) was 5.1% and the NSB 2.0% in the experiment shown; in other experiments specific binding was between 4 and 9%, and the NSB varied from 0.5 to 2%. The displacement curve is expressed in terms of the ratio of specific binding at a given dose (B) to the specific binding in the absence of added β TG (B_0) plotted on a logistic scale²¹; each point represents the mean of four determinations, and the bars 1 s.d. There was no displacement of 125 I- β TG by PF_4 (100 μ g ml^{-1}), hen egg lysozyme (100 μ g ml^{-1}) or human leukaemia lysozyme (100 μ g ml^{-1}). Inset: Scatchard plot derived from the displacement curve shown. The dissociation constant (K_d) was estimated as 2.3×10^{-7} (95% confidence limits, 1.7–2.9) and the number of receptors per endothelial cell at 2.6×10^6 (95% confidence limits, 2.1–3.1 $\times$ 10⁶). B/F, Bound/free β TG.

This effect of β TG suggested that the endothelial cell might possess a cell-surface receptor for β TG. The experiment shown in Fig. 1 indicates the presence of a specific receptor for β TG on bovine aortic endothelial cells. Competition for binding of 125 I-labelled β TG was by β TG only and not by PF_4 in several-fold excess, nor by other basic proteins, such as hen egg lysozyme (Worthington) or human leukaemic lysozyme¹⁴. The concentrations of β TG required for half-maximal inhibition of binding are similar to those required to inhibit PGI_2 formation by endothelial cells. In four separate experiments, the average dissociation constant (K_d) was 1.7×10^{-7} M and the number of receptors per cell was calculated as 2×10^6 .

Although the methods used to measure the β TG response in endothelial cells do not enable us to relate the effect directly to the binding to endothelial cells, nevertheless, the co-existence of

a specific binding site and the biological effect strongly suggests that the two are related. Apart from studies of drugs¹⁰, there is little information on other factors which might regulate PGI₂ production by endothelial cells. MacIntyre *et al.*¹⁵ found that a factor in cell-free plasma stimulated PGI₂ production by pig aortic endothelial cells. Thrombin, trypsin and a calcium ionophore have been shown to stimulate PGI₂ production¹⁶, and in experiments similar to our own, plasma low-density lipoproteins have been found to decrease production of PGI₂ activity by human umbilical vein endothelial cells¹⁷. The present results suggest that β TG may be involved in the control of haemostasis. During vascular wall injury, which is followed by platelet adhesion and aggregation—processes which would both be inhibited by PGI₂—release of β TG could prevent PGI₂ formation by adjacent endothelium, and allow the healing process to continue. In this situation β TG would be acting locally, and the dissociation constant derived from our experiments would be consistent with this action, as concentrations of this order are exceeded during platelet aggregation and release¹³. A local mode of action requires a binding site with an affinity some orders of magnitude less than the normal plasma level of 20 ng ml⁻¹ (approximately 0.7 nM)¹³. Bovine endothelial cells were washed free of fetal calf serum before use in the experiments described above. Although bovine β TG has not been reported it is likely that such a protein exists. In this case, although the measured affinity suggests that a significant proportion of bound β TG would dissociate during the washing procedure, the activities measured here may be diminished to some extent by residual occupancy of receptor sites.

It is of particular interest that the distinct but closely related platelet protein, PF4 (ref. 3), neither competes for receptor binding nor has a similar biological effect. β TG has been isolated in two different forms, the preparation used in these experiments corresponding to that originally described by Moore *et al.*¹, its structure has been completely determined³. The other preparation, which has been designated low-affinity PF4 (LA-PF4) by Rucinski *et al.*¹⁸, and has an additional NH₂-terminal tetrapeptide but is otherwise identical to β TG, needs to be investigated for probable similar activity. Finally, if β TG interaction with receptor is linked to the effects of the protein on PGI₂ formation, it is important to determine precisely the biochemical events occurring between receptor interaction and PGI₂ production in endothelial cells.

We thank Dr R. E. Canfield for a gift of human leukaemia lysozyme. This work was supported by grants from the National Health and MRC, the National Heart Foundation of Australia, and the Australian Tobacco Research Foundation.

Received 5 June; accepted 12 September 1979.

1. Moore, S., Pepper, D. S. & Cash, J. D. *Biochim. biophys. Acta* **379**, 360–369, 370–384 (1975).
2. Moore, S. & Pepper, D. S. in *Platelets in Biology and Pathology* (ed. Gordon, J. L.) 293 (North-Holland, Amsterdam, 1977).
3. Begg, G. S., Pepper, D. S., Chesterman, C. N. & Morgan, F. J. *Biochemistry* **17**, 1739–1744 (1978).
4. Moncada, S., Gryglewski, R., Bunting, S. & Vane, J. R. *Nature* **263**, 663–665 (1976).
5. Gryglewski, R. J., Bunting, S., Moncada, S., Flower, R. J. & Vane, J. R. *Prostaglandins* **12**, 685–713 (1976).
6. Bunting, S., Gryglewski, R., Moncada, S. & Vane, J. R. *Prostaglandins* **12**, 897–913 (1976).
7. Best, L. C., Martin, T. J., Russell, R. G. G. & Preston, F. E. *Nature* **267**, 850–852 (1977).
8. Gorman, R. R., Bunting, S. & Miller, O. V. *Prostaglandins* **13**, 377–388 (1977).
9. Tateson, J. E., Moncada, S. & Vane, J. R. *Prostaglandins* **13**, 389–397 (1977).
10. Baenziger, N. L., Dillender, M. J. & Majerus, P. W. *Biochem. biophys. Res. Commun.* **78**, 294–301 (1977).
11. Weksler, B. B., Marcus, A. J. & Jaffe, E. A. *Proc. natn. Acad. Sci. U.S.A.* **74**, 3922–3926 (1977).
12. Gimbrone, M. A., Cotran, R. S. & Folkman, J. *J. Cell Biol.* **60**, 673–684 (1974).
13. Ludlam, C. A., Moore, S., Bolton, A. E., Pepper, D. S. & Cash, J. E. *Thromb. Res.* **6**, 543–548 (1975).
14. Canfield, R. E., Kammerman, S., Sobel, J. H. & Morgan, F. J. *Nature new Biol.* **232**, 16–17 (1971).
15. MacIntyre, D. E., Pearson, J. D. & Gordon, J. L. *Nature* **271**, 549–551 (1978).
16. Weksler, B. B., Ley, C. W. & Jaffe, E. W. *J. clin. Invest.* **62**, 923–930 (1978).
17. Nordøy, A., Svensson, B., Wiebe, D. & Hoak, J. C. *Circulation Res.* **43**, 527–534 (1978).
18. Rucinski, B., Niewiarowski, S., Prance, J., Walz, D. A. & Budzynski, A. Z. *Blood* **43**, 47–62 (1979).
19. Morgan, F. J., Chesterman, C. N., McGready, J. R. & Begg, G. S. *Haemostasis* **6**, 53–58 (1977).
20. Chesterman, C. N., McGready, J. R., Doyle, D. J. & Morgan, F. J. *Br. J. Haemat.* **40**, 489–500 (1978).
21. Rodbard, D. *Clin. Chem.* **20**, 1255–1270 (1974).

Inhibition of platelet thrombus formation by chlorpromazine acting to diminish haemolysis

G. V. R. Born

Department of Pharmacology, King's College, London WC2, UK

A. Wehmeier

Department of Pharmacology, University of Cambridge, Cambridge, UK

There is increasing evidence¹ that the sudden, unpredictable event initiating myocardial infarction is fissuring of an atherosclerotic plaque. The resulting haemorrhage into the arterial wall produces obstructive platelet thrombi, just as arterial haemorrhages elsewhere produce haemostatic platelet plugs. It has been suggested¹ that such platelet aggregation depends on ADP originating in red cells which are subjected to excessive haemodynamic stress at the site of haemorrhage. The release of ADP from red cells has been demonstrated *in vitro* in equivalent conditions of shear stress^{2,3}; and other mechanisms, such as activation by collagen, cannot account for the rapidity with which the platelets react⁴. One of us (G.V.R.B.) has suggested that drugs capable of counteracting haemolysis⁵ might diminish the activating effect of erythrocytes on platelets⁶ and so inhibit their aggregation as thrombi. Thus, chlorpromazine, added to human blood at concentrations which diminish haemolysis but do not directly affect platelet aggregation^{7,8}, prolonged the 'bleeding time' from small holes in artificial vessels where extravasation is terminated, as in living arterioles, by aggregated platelets⁹. The bleeding time was also prolonged by apyrase, consistent with the conclusion that the chlorpromazine acted through decreasing plasma ADP. We show here that this occurs through the anti-haemolytic action of chlorpromazine.

Venous blood was obtained from apparently healthy volunteers who had not taken drugs known to affect platelet reactions. The blood with heparin (20 or 50 units ml⁻¹) as anticoagulant was pumped at 37 °C from a syringe through polyethylene tubing of 280 μ m internal diameter and 50 cm long. The flow rate was 0.17 or 0.21 ml min⁻¹ (both rates gave the same results) and the pressure was about 300 mm Hg. The duration of 'bleeding' from a small cut through about one half of the circumference of the tube and 30 cm from its end was determined up to 600 s. Free haemoglobin was determined by the cyan-methaemoglobin method in blood from the syringe ('unsheared') and from the end of the tube ('sheared'). Most determinations on unsheared blood were bracketed between two on sheared blood.

It was confirmed⁹ that chlorpromazine added to the syringe blood for 45 min prolonged the bleeding time significantly, and did so more at 5 or 10 μ M than at 50 μ M (Table 1).

Unsheared blood contained low concentrations of free haemoglobin which were not changed significantly by chlorpromazine at 5 or 10 μ M but were increased by drug concentrations of 50 μ M (Table 1). In sheared blood free haemoglobin concentrations were significantly higher than in unsheared blood in the absence of chlorpromazine, which decreased the free haemoglobin significantly at 5 μ M and just significantly at 10 μ M but not at 50 μ M. The differences in free haemoglobin between unsheared and sheared blood were decreased highly significantly by chlorpromazine but less at 50 μ M than at 5 or 10 μ M.

Our interpretation that the prolongation of bleeding time by chlorpromazine depends on its effect on red cells is tenable only if direct inhibition of platelet aggregation could be excluded. In three experiments it was confirmed (see ref. 8) that chlorpromazine incubated at these concentrations in blood or pla-

Table 1 Effect of chlorpromazine on bleeding times and haemolysis of heparinised blood during its shear-flow through artificial vessels

No. of determinations		Chlorpromazine concentration (μM)	Bleeding time (s) mean s.e.m.	Free haemoglobin (mg per 100 ml) in blood		
Unsheared	Sheared			Unsheared mean s.e.m.	Sheared mean s.e.m.	Difference mean s.e.m.
15	15	0 (Controls)	178 $\pm$ 23	33.4 $\pm$ 1.4	44.6 $\pm$ 2.2	11.2 $\pm$ 1.9
14	14	5	242 $\pm$ 28*	32.3 $\pm$ 3.5	35.9 $\pm$ 3.5	3.6 $\pm$ 0.9 ⁺
14	14	10	288 $\pm$ 32*	37.2 $\pm$ 2.8	38.1 $\pm$ 3.3	0.9 $\pm$ 1.1 ⁺
15	15	50	263 $\pm$ 30*	41.3 $\pm$ 3.8	44.7 $\pm$ 3.9	3.4 $\pm$ 2.1 ⁺

Significances of differences from controls: * $P < 0.05$; ⁺ $P < 0.005$.

telet-rich plasma for increasing lengths of time had no significant effect on the velocity of primary aggregation¹⁰ induced by ADP. Secondary aggregation associated with the release reaction is not inhibited by chlorpromazine at 5 μM , slightly at 10 μM and more at 50 μM (ref. 8), whereas the bleeding time was more prolonged and haemolysis more strongly inhibited at 5 μM and 10 μM than at 50 μM .

These observations establish that low concentrations of chlorpromazine greatly diminish haemolysis of blood during shear-flow but not when at rest. This strongly supports the proposition⁹ that chlorpromazine increases the bleeding time through its anti-haemolytic effect. In the absence of chlorpromazine, haemolysis would have given initial plasma concentrations of ADP and ATP of 0.05 and 0.40 μM respectively. Because the dephosphorylation in blood of ATP to ADP is much faster than that of ADP to AMP¹¹, the concentration of ADP was probably higher and amply sufficient to activate platelets¹². It can be concluded, therefore, that ADP released from red cells lysed by haemorrhagic shear-flow can account for haemostatic and thrombotic platelet aggregation.

The haemolysis caused by shear-flow was strikingly decreased by chlorpromazine. On the assumption that these decreases in the release of haemoglobin were accompanied by corresponding decreases in the release of ADP and ATP, it may be concluded that the increases in bleeding time brought about by these concentrations of chlorpromazine are explained by the very much lower concentrations of ADP available for activating the platelets.

This explanation is supported by the apparently paradoxical diminutions in the effect on both bleeding time and haemolysis when chlorpromazine was present at the higher concentration of 50 μM . Chlorpromazine, like other drugs (see ref. 5), is anti-haemolytic at low but strongly haemolytic at higher concentrations. It seems, therefore, that in our experiments chlorpromazine at 10 μM was almost maximally anti-haemolytic whereas at 50 μM the opposing haemolytic effect began to show itself also.

While the blood was in the syringe reservoirs at 37 °C it haemolysed to a small extent (0.23 $\pm$ 0.02% in blood from 8 donors) after 2–3 h. In such a long time the adenine nucleotides released from lysed red cells are enzymatically dephosphorylated¹¹ so that there would be no free ADP to activate the platelets in the blood reservoirs.

Red cells undergo the greatest haemodynamic stress near the vessel walls, where flow velocity is slowest. Therefore, the concentration of released ADP is greatest near the walls which is where the platelets have to be activated for their haemostatic function.

The wall shear stress in these artificial vessels was about 50 dyn cm⁻², which is similar to that in living arterioles¹³. This stress, even when acting for considerably more than 10 s, is too small to activate platelets directly¹⁴. The wall shear stress is higher by at least two orders of magnitude at sites of arterial haemorrhage³. This stress is too brief to activate platelets directly¹⁴. Their activation can now be accounted for by assuming the local lysis of a very small proportion of red cells.

There is evidence^{15,16} which can be interpreted¹⁷ to suggest that chlorpromazine and at least one other phenothiazine administered for clinical purposes are capable of protecting against myocardial infarction. As the concentration of chlorpromazine in patients' plasma¹⁸ is about one order of magni-

tude lower than that which greatly prolonged the *ex vivo* bleeding time, blood concentrations of chlorpromazine produced clinically may protect against myocardial infarction by the anti-haemolytic mechanism.

All this evidence supports the suggestion^{1,9,17} that drugs which have the effect described in this paper for chlorpromazine may be found to ameliorate or prevent arterial, for example coronary, thrombosis when it is induced by haemorrhage into atheromatous lesions or by other haemodynamic stresses severe enough to cause haemolysis.

We thank Miss Margaret Hickman for technical assistance, the German National Scholarship Foundation for supporting A.W. and the Fritz Thyssen Foundation for supporting this research.

Received 26 June; accepted 25 September 1979.

1. Born, G. V. R. *Arterial Thrombosis and its Prevention* (Excerpta Medica, Amsterdam, in the press).
2. Schmid-Schönbein, H. *et al. Bioreheology* (in the press).
3. Schmid-Schönbein, H., Rieger, H., & Fischer, T. *Blood Vessels: Problems Arising at the Borders of Natural and Artificial Blood Vessels* (eds Effert, S. & Meyer-Erkelenz, J. D.) 57–63 (Springer, Berlin, 1977).
4. Born, G. V. R. *Br. med. Bull.* **33**, 193–197 (1977).
5. Seaman, P. *Pharmac. Rev.* **24**, 583–655 (1972).
6. Gaarder, A., Jonsen, J., Laland, S., Hellem, A. & Owren, P. *Nature* **192**, 531–533 (1961).
7. Ahtee, L. & Paasonen, M. K. *J. pharm. Pharmac.* **18**, 126–128 (1966).
8. Mills, D. C. B. & Roberts, G. C. K. *Nature* **213**, 35–38 (1967).
9. Born, G. V. R., Bergqvist, D. & Afors, K. *-E. Nature* **259**, 233–236 (1976).
10. Born, G. V. R. *Nature* **194**, 927–929 (1962).
11. Haslam, R. J. & Mills, D. C. B. *Biochem. J.* **103**, 773–784 (1967).
12. Milton, J. C., Yung, W., Glushak, C. & Frojmovic, M. M. *Can. J. Physiol. Pharmac.* (in the press).
13. Schmid-Schönbein, H. *Handbuch der allgemeinen Pathologie*, **111–117** (ed. Meesen, H.) 289–384 (Springer, Heidelberg, 1977).
14. Colantuoni, G., Hellums, J. D., Moake, J. L. & Alfrey, C. P. *Trans. Am. Soc. artif. Internal Organs* **23**, 626–630 (1977).
15. Ödegård, Ö. *Acta genet. (Basel)* **17**, 137–153 (1967).
16. Davidsen, O., Lindeneg, O. & Walsh, M. *Acta med. scand.* **205**, 191–194 (1979).
17. Born, G. V. R. *Lancet* **i**, 822 (1979).
18. Mackay, A. V. P., Healey, A. F. & Baker, J. *Br. J. clin. Pharmac.* **1**, 425–430 (1974).

Electron microscope evidence for an 80 Å unit in collagen fibrils

D. A. D. Parry

Department of Chemistry, Biochemistry and Biophysics, Massey University, Palmerston North, New Zealand

A. S. Craig

Applied Biochemistry Division, DSIR Palmerston North, New Zealand

Connective tissues are composite structures containing collagen, elastin, glycosaminoglycans, minerals, water and other minor components^{1,2}. In all cases the collagen exists predominantly in fibrillar form. The size distribution of the fibrils does, however, vary markedly with both age and the mechanical requirements of the tissue³. Little is known about the mechanism of fibril formation *in vivo*, although some information is now available from *in vitro* polymerisation studies⁴. We have now collected new and extensive electron microscope data on the size of collagen fibrils from tendon, skin, cornea and other tissues from both fetal and immature animals. The results reported here show that the diameters of the collagen fibrils thus measured lie close to a multiple of 80 Å, a result which may be simply and readily interpreted in terms of the collagen microfibril and its mode of packing.

Table 1 Classification of the mean diameters of collagen fibrils having sharp unimodal populations

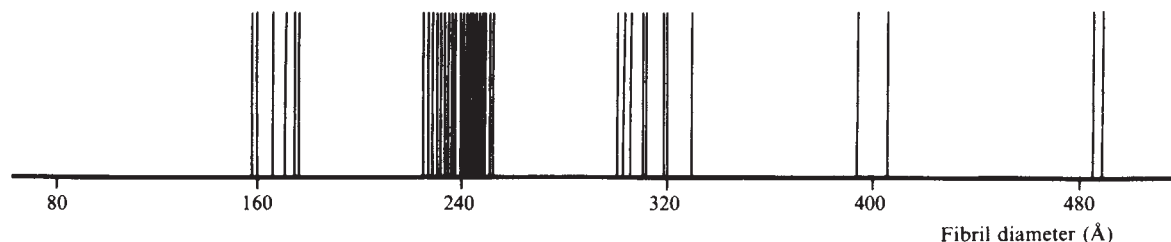
Tissue	Species	Age*	Collagen fibril diameter $n \cdot 80 \text{ \AA}$				
			$n = 2$	$n = 3$	$n = 4$	$n = 5$	$n = 6$
Tendon: Triceps	Rat	0 day	160				
	Triceps	Rat	0 day	250			
	Tail	Rat	18 day F	230			
	Tail	Rat	0 day		305		
	Tail	Rat	<1 day				485
	Upper forelimb	Rat	18 day F		320		
	Forelimb digital flexor	Rat	18 day F	230			
	Forelimb digital flexor	Rat	0 day		310		
	Hindlimb digital flexor	Rat	18 day F	175			
	Hindlimb digital flexor	Rat	5 day			405	
	Forelimb	Sheep	60 day F	245			
	Forelimb	Sheep	60 day F		305		
	Hindlimb	Sheep	60 day F		330		
	Hindlimb digital flexor	Sheep	72 day F			395	
	Hindlimb digital extensor	Sheep	72 day F				490
Cornea (a) Cartilaginous fish	Dogfish	A		245			
	Elephant fish	A		245			
	Stingray	A		235			
	(b) Bony fish	Butterfish	A	160			
		Moki	A	165			
	(c) Amphibians	Salamander	A		235		
		Toad	A		230		
	(d) Reptiles	Turtle	A		235		
	(e) Birds	Kiwi	A		245		
	(f) Mammals	Opossum	A		245		
		Rat	18 day F	175			
		Rat	0 day		225		
		Rat	A		235		
		Rabbit	A		250		
		Human	14 and 24 week F	170			
		Human	73 year		225		
Skin	Rat	18 day F		240			
	Rat	0 day			320		
	Sheep	60 and 72 day F			300		
	Human	14 week F		250			
Endoneurium: Sciatic nerve	Rat	0 day		240			
	Rat	5 day			310		
Paratenon: Tail tendon	Rat	0 day		245			

* A, Adult; F, fetal.

It is generally accepted that collagen fibrils are constructed from molecules which are axially staggered with respect to one another by about $668 \text{ \AA}$ (or a multiple thereof)⁵⁻⁹. The nature of the lateral packing of the molecules is controversial, however. The first significant packing model proposed was that of Smith¹⁰, who suggested that a five-stranded microfibril of diameter $\sim 35 \text{ \AA}$ could exist in connective tissues. Improved X-ray data from orientated specimens of moist rat-tail tendon subsequently became available and these confirmed that a unit of diameter $\sim 38 \text{ \AA}$ was indeed present¹¹, thus providing strong support for the Smith microfibril. Further interpretation of the X-ray patterns¹²⁻¹⁴ showed that the unit cell was a slightly sheared tetragonal cell of lateral side $\sim 77 \text{ \AA}$ and that each unit cell contained four microfibrils related to one another by a 4_3 screw axis. Others have since suggested alternative schemes for the packing of collagen molecules in the fibril (see for example refs 15-17) and in each instance it is claimed that the X-ray data are consistent with the proposed scheme. Electron microscope evidence has therefore been sought to differentiate between the various models which have been put forward. At the present time, however, no conclusive evidence has been obtained from

transverse sections which supports a regular arrangement of collagen molecules or groupings of collagen molecules though the possibility remains that the preparative procedures used have not preserved the *in vivo* lattice structure.

It has been suggested by Fraser *et al.*¹⁸ that if the structure of small collagen fibrils, which appear circular in section, is indeed based on a lateral repeating unit of four microfibrils related to one another by a 4_3 screw axis, then their diameters should be multiples of about $85 \text{ \AA}$. This value is calculated on the basis of the most symmetrical arrangement of lateral repeating units, that is, an $n \times n$ array. Fraser *et al.*¹⁸ noted that the preservation of the structure of small fibrils would probably be insufficient to distinguish between $n \times n$ unit cell fibrils and helical fibrils, both of which would appear to be circular in cross-section. Parry *et al.*¹⁹ simultaneously reported that the mean diameter of the collagen fibrils from 10 tissues, each of which had a sharp unimodal distribution of fibril diameters, occurred at multiples of about $80 \text{ \AA}$. We present new data which support those preliminary observations and which imply that the unit cell and microfibrillar structure proposed for tendon are likely to be a feature of all other connective tissues as well.

**Fig. 1** Graphical representation of the values listed in Table 1. It can be seen that the diameters of the collagen fibrils fall in discrete clusters separated from one another by $80 \text{ \AA}$. The clusters are centred on values of about 160, 240, 320, 400 and $480 \text{ \AA}$.

Let us consider the conditions in which quantum jumps of 80 Å in fibril diameter might most easily be observed. Firstly, the magnification of the electron microscope must be known precisely for each set of micrographs taken, the calibration being based, say, on a replica grating. Secondly, the mean value of many diameter measurements (≥ 100) taken from the original electron micrographs using a binocular microscope, will only be close to the true diameter of each and every fibril (and hence be meaningful) if the distribution of collagen fibril diameters is both unimodal and sharp. This assumes that the spread of measured values does not represent the true range of collagen fibril diameters but arises entirely from the inherent difficulty of measuring and defining the fibril periphery after standard electron microscopic preparative procedures have been used.

The standard deviation for each distribution of collagen fibril diameters has been calculated and where this is < 35 Å it has been considered that the distribution is sufficiently sharp to represent a population of uniform diameter fibrils. The stipulated standard deviation, being less than $(80/2)$ Å, gives a criterion on which to exclude those fibril diameter distributions which are likely to be comprised of two or more populations of fibrils differing in diameter from one another by a multiple of 80 Å. Such distributions will have a mean diameter dependent solely on the relative proportions of the various populations of fibrils making up the overall distribution.

Measurements made in this work, together with those of Parry *et al.*¹⁹, are shown in Table 1 and Fig. 1. The results show that the diameters of small collagen fibrils taken from a variety of diverse connective tissues have values which are close to a multiple of about 80 Å. It is important to note that Table 1 contains every piece of data that we have collected, subject only to it satisfying the stated criteria. We are aware of many values quoted in the literature which relate to the diameters of small collagen fibrils and while many of these values fall close to a multiple of 80 Å (see for example ref. 20), others do not. We believe that it is probable that most, if not all, of these values do not satisfy one or both of the criteria listed earlier.

It therefore seems appropriate to suggest that the 80 Å unit cell first seen in tendon from X-ray diffraction analyses and now shown by electron microscopy to exist also in tissues such as skin, cornea and endoneurium, as well as tendon, may have a similar interpretation in all cases, that is, each 80 Å unit contains four microfibrils related to one another by a 4_3 screw axis.

We believe that the diameters of all collagen fibrils, irrespective of their size, may be multiples of about 80 Å. This cannot, of course, be easily proved in the cases of broad distributions of collagen fibrils as a meaningful mean diameter (within the limits imposed by our criteria) can no longer be calculated and also because any slight ellipticity of a single fibril in cross-section will disguise its true diameter. Also the shape of the collagen fibrils in cross-section often become less regular as the fibrils increase in diameter and as the tissue ages^{21,22}. Nonetheless we propose, on the basis of these results, that all fibril diameter distributions, whether they originate from a fetal, mature or senescent tissue, are constructed from changing populations of collagen fibrils whose diameters are multiples of about 80 Å.

Received 25 June; accepted 3 September 1979.

- Mathews, M. B. in *Molecular Biology, Biochemistry and Biophysics* Vol. 19 (Springer, Berlin, 1975).
- Hall, D. A. *The Ageing of Connective Tissue* (Academic, London, 1976).
- Parry, D. A. D., Barnes, G. R. G. & Craig, A. S. *Proc. R. Soc. B* **203**, 305–321 (1978).
- Treistad, R. L., Hayashi, K. & Gross, J. *Proc. natn. Acad. Sci. U.S.A.* **73**, 4027–4031 (1976).
- Hodge, A. J. & Schmitt, F. O. *Proc. natn. Acad. Sci. U.S.A.* **46**, 186–197 (1960).
- Hodge, A. J. & Petruska, J. A. in *Aspects of Protein Structure* (ed. Ramachandran, G. N.) 289–300 (Academic, New York, 1963).
- Hulmes, D. J. S., Miller, A., Parry, D. A. D., Piez, K. A. & Woodhead-Galloway, J. *J. molec. Biol.* **79**, 137–148 (1973).
- Chapman, J. A. & Hardcastle, R. A. *Connect. Tissue Res.* **2**, 151–159 (1974).
- Doyle, B. B. *et al. Proc. R. Soc. B* **186**, 67–74 (1974).
- Smith, J. W. *Nature* **219**, 157–158 (1968).
- Miller, A. & Wray, J. S. *Nature* **230**, 437–439 (1971).
- Miller, A. & Parry, D. A. D. *J. molec. Biol.* **75**, 441–447 (1973).
- Fraser, R. D. B., Miller, A. & Parry, D. A. D. *J. molec. Biol.* **83**, 281–283 (1974).
- Fraser, R. D. B. & MacRae, T. P. *J. molec. Biol.* **127**, 129–133 (1979).
- Hosemann, R., Dreissig, W. & Nemetschek, T. *J. molec. Biol.* **83**, 275–280 (1974).

- Woodhead-Galloway, J., Hukins, D. W. L. & Wray, J. S. *Biochem. biophys. Res. Commun.* **64**, 1237–1244 (1975).
- Hukins, D. W. L. & Woodhead-Galloway, J. *Molec. Cryst. Liq. Cryst.* **41**, 33–39 (1977).
- Fraser, R. D. B., MacRae, T. P. & Suzuki, E. in *Fibrous Proteins: Scientific, Industrial and Medical Aspects* Vol. 1 (eds Parry, D. A. D. & Creamer, L. K.) 179–206 (Academic, London, 1979).
- Parry, D. A. D., Craig, A. S. & Barnes, G. R. G. (1979) in *Fibrous Proteins: Scientific, Industrial and Medical Aspects* Vol. 2 (eds Parry, D. A. D. & Creamer, L. K.) 77–88 (Academic, London, 1979).
- Jackson, S. F. *Proc. R. Soc. B* **144**, 556–572 (1956).
- Parry, D. A. D. & Craig, A. S. *Biopolymers* **17**, 843–855 (1978).
- Parry, D. A. D., Craig, A. S. & Barnes, G. R. G. *Proc. R. Soc. B* **203**, 293–303 (1978).

Competence for genetic transformation in pneumococcus depends on synthesis of a small set of proteins

D. A. Morrison & M. F. Baker

Department of Biological Sciences, University of Illinois at Chicago Circle, Chicago, Illinois 60680

In bacterial genetic transformation the uptake of DNA and its integration into the resident chromosome is dependent on a special cellular state, termed competence. In those species where appearance of competence has been studied, specific (but often poorly defined) growth conditions lead to a simultaneous development of competence in a substantial fraction of the cells in a culture. In *Bacillus subtilis*^{1–4}, and in *Haemophilus* species^{5,6}, competence appears in the stationary phase of growth or in certain other growth-limiting conditions^{5,6}. *Streptococcus pneumoniae* (pneumococcus) is perhaps unusual in that virtually all cells of a culture become competent^{7,8}, for a short period at a specific cell density during logarithmic growth, without perturbing the growth rate⁹. The synchronous appearance of competence in pneumococcal cultures results from an auto-catalytic effect of a small protein¹⁰ released by the cells that induces competence^{11,12}. The response to competence factor has been shown to require protein synthesis¹³. We report here additional information on the nature of competence in pneumococcus: pulse-labelling studies show that for the brief period of competence protein synthesis is restricted to a few specific polypeptides.

Figure 1 displays the patterns of proteins pulse-labelled with ³⁵S-methionine at successive intervals before, during, and after competence in a culture transferred to a low-methionine labelling medium after stimulation by endogenous competence factor. Also shown is the level of competence achieved by the end of each labelling pulse, measured genetically. The fluorogram reveals two prominent features of protein synthesis associated with the appearance of competence. First, there is a striking decrease in the synthesis of most proteins, including all the major labelled bands. Second, during the middle portion of the competence period, protein synthesis, although normal in total amount, is limited to about 11 principal species. The approximate molecular weights of these are: 14.5K, 16K, 18K, 19.5K, 31K, 34K, 36K, 41K, 45K, 50K, and 52K. Only one of these, about 19,500 MW, is clearly absent from the pattern of non-competent cells at this level of resolution. Critical comparison of lanes in the original film suggests that at least three others are new, but a second dimension will be needed to verify this. Thereafter, as competence declines, the labelling of these bands decreases, and synthesis of the normal complement of proteins resumes.

In a second experiment, the synthesis of the same set of proteins appeared in samples of a culture that became competent, but not in samples of a parallel culture grown with trypsin to inactivate the intercellular action of competence factor (Fig. 2).

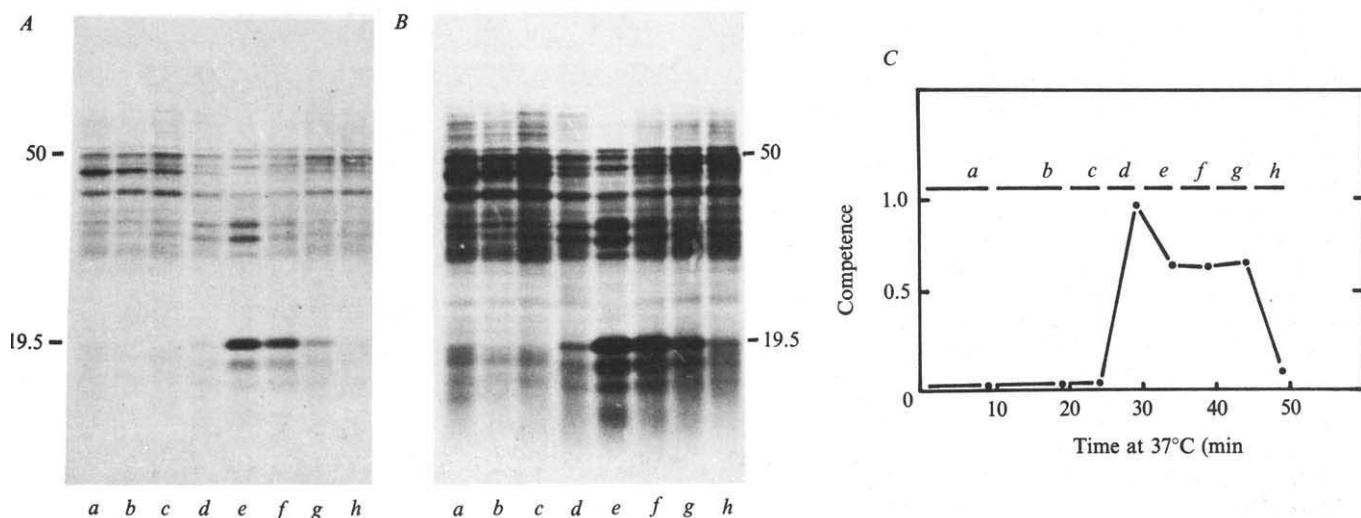


Fig. 1 Pulse-labelled proteins of a pneumococcal culture developing competence for genetic transformation. A growing culture of DP1700 was chilled about 25 min before the peak of competence, concentrated to 4×10^8 colony-forming units per ml and frozen¹⁴. A sample was thawed at 0 °C, washed and resuspended in an equal volume of labelling medium¹⁶. During incubation of this sample at 37 °C, aliquots were labelled with ³⁵S-methionine ($12 \mu\text{Ci ml}^{-1}$) for periods, shown by bars in panel C, then assayed for competence by dilution of a portion into broth containing $2 \mu\text{g ml}^{-1}$ Ery-r transforming DNA, and prepared for electrophoresis. Cells were chilled, washed, and resuspended in 10 mM Tris, pH 6.8, 1 mM EDTA, 5 mM MgCl₂, 0.1% Triton X-100, $10 \mu\text{g ml}^{-1}$ DNase I, $50 \mu\text{g ml}^{-1}$ RNase, and lysed at 37 °C (10 min). Lysates, boiled with 1% mercaptoethanol and SDS, were applied to a 12% slab gel. The $0.15 \times 10 \times 14$ cm polyacrylamide gel used the SDS disc buffer system of Laemmli¹⁷, and fluorography was as described by Laskey and Mills¹⁸, with Kodak Xomat XR-1 film. Each well of the slab gel contained 10^4 c.p.m. incorporated ³⁵S. A, Fluorogram of samples labelled for the periods indicated in C, 6-h exposure. B, Same as A at 18-h exposure. C, Course of competence development. Maximum competence represents 10^6 Ery-r transformants per ml per μg DNA, after a 7-min uptake period at 25 °C. Molecular weights were determined from positions of reference proteins listed in text. (Strain DP1700 is a derivative of Rx-1 carrying the *end-1 exo-2* mutations isolated in R₆ by Lacks¹⁹, and was supplied by N. S. Shoemaker. In our hands it exhibits a tendency to lyse if handled soon after competence^{11,12}, seen here as low recovery of ³⁵S in sample d of Fig. 2. Such lysis did not occur in any of the samples of Fig. 1, as shown by complete recovery of incorporated radioactivity, and by Coumassie blue staining after electrophoresis.)

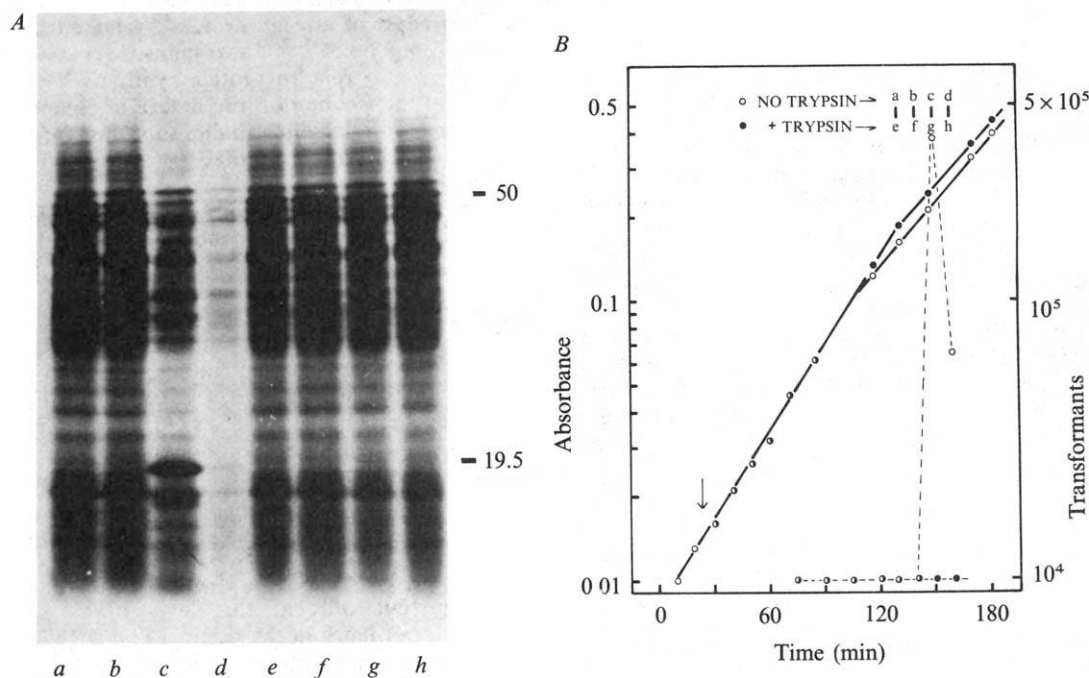


Fig. 2 Effect of trypsin on competence development and on protein synthesis patterns. A culture of DP1700 growing at 37 °C in competence medium¹⁴ was split at the time indicated by the arrow and one half was supplemented with trypsin to $20 \mu\text{g ml}^{-1}$ (gel lanes e-h). The other half was an untreated control (gel lanes a-d). Growth was monitored at 430 nm in the Coleman jr II spectrophotometer. At intervals, samples were removed, chilled, frozen, thawed, transferred to labelling medium containing $2 \mu\text{Ci ml}^{-1}$ ³⁵S-methionine, and incubated at 37 °C for 20 min. A portion of each sample was then assayed for competence, and the rest prepared for electrophoresis and analysed, as in Fig. 1. Panel A, fluorogram of gel for samples taken at the times indicated in panel B, a-d control, e-h trypsin treated. Panel B, culture growth and competence assays. ●, Trypsin treated; ○, control; —, optical density of culture; ----, competence.

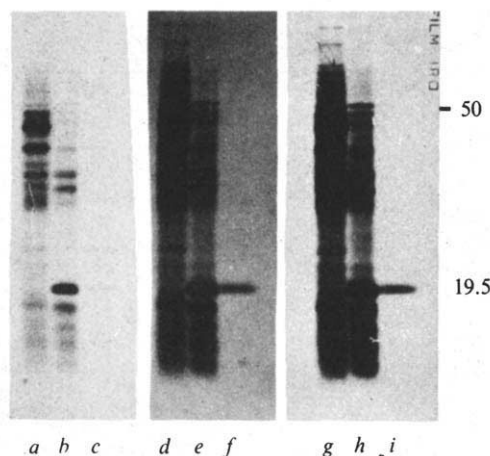


Fig. 3 Comparison of pulse-labelled proteins with purified eclipse complex protein. A lysate of component cells (*b*) labelled as in Fig. 1 (pulse *e*), was analysed on a slab gel as in Fig. 1. Adjacent lanes contained: *c*, protein obtained from ^{35}S -methionine-labelled eclipse complex purified as described elsewhere¹⁴; and *a*, a lysate of pulse-labelled non-competent cells. Three fluorography exposures are shown: *a-c*, 6 h; *d-f*, 12 h; and *g-i*, 18 h.

We suggest that this event, coinciding precisely with the appearance of competence, may represent the coordinated synthesis of sufficient amounts of the proteins involved in uptake and/or recombination of DNA to accomplish the rapid uptake and integration of large amounts of DNA.

Figure 3 compares the proteins labelled specifically at competence with the protein which coats donor DNA in the competent cell during eclipse, after uptake and before integration into the chromosome^{14,15}. The principal competence-specific band co-migrated precisely with pure eclipse complex protein, and may consist wholly of that DNA-binding protein. By comparison with standards of BSA (MW 66,000), trypsinogen (MW 25,000), β -lactoglobulin (MW 18,400) and lysozyme (MW 14,000), we estimate the MW of this polypeptide to be $19.5 \pm 0.5 \times 10^3$, a value somewhat larger than that estimated previously¹⁵ in an analysis heavily dependent on the mobility of cytochrome *c*.

The competence-specific 19,500 MW protein and the 19,500 MW protein of eclipse complex have not yet been directly shown to be identical; however, the correlation with competence of synthesis of the former, the binding of the latter to transforming DNA in the cell, and their identical electrophoretic mobilities strongly suggest that they will ultimately be found so.

Evidence on the nature of the competent state in any species is limited. One extreme hypothesis is that competence reflects simply the acquisition of a transport system for DNA, with constitutive proteins of nucleic acid metabolism carrying out the remaining steps. On this view, the mechanism of integration could simply represent the ordinary fate of free homologous intracellular strands of DNA. At another extreme is the hypothesis that during ordinary nucleic acid metabolism the reactions required for genetic transformation are unusual, and that competence, then, requires the coordinated synthesis of specific proteins not usually present in sufficient quantity to carry out these reactions. The elaborate shift to the synthesis of few proteins that we report here accompanies competence certainly suggests the possibility of the latter case.

Clearly, specific assignments of roles in transformation to these apparently competence-specific proteins will depend on further research involving a combination of genetic and biochemical approaches. The major competence-specific protein, 19.5, of course, is already apparently implicated by its binding to DNA in eclipse. If even a few others should also be identified, then pneumococcal competence would constitute a particularly

clear example of an inducible bacterial system for genetic recombination.

This work was supported in part by a grant from the NSF.

Received 25 May; accepted 23 August 1979.

1. Nester, E. W. *J. Bact.* **87**, 867-875 (1964).
2. Bott, K. F. & Wilson, G. A. *Bact. Rev.* **32**, 370-378 (1968).
3. Wilson, G. A. & Bott, K. F. *J. Bact.* **95**, 1439-1449 (1968).
4. Dooley, D. C., Hadden, C. T. & Nester, E. W. *J. Bact.* **108**, 668-679 (1971).
5. Goodgal, S. & Herriott, R. M. *J. gen. Physiol.* **44**, 1201-1227 (1961).
6. Spencer, H. T. & Herriott, R. M. *J. Bact.* **90**, 911-920 (1965).
7. Javor, G. T. & Tomasz, A. *Proc. natn. Acad. Sci. U.S.A.* **68**, 1216-1222 (1968).
8. Porter, R. D. & Guild, W. R. *J. Bact.* **97**, 1033-1035 (1969).
9. Tomasz, A. *Nature* **208**, 155 (1965).
10. Tomasz, A. & Mosser, J. L. *Proc. natn. Acad. Sci. U.S.A.* **55**, 58-66 (1966).
11. Tomasz, A. & Hotchkiss, R. D. *Proc. natn. Acad. Sci. U.S.A.* **51**, 480-487 (1964).
12. Seto, H. & Tomasz, A. *J. Bact.* **121**, 344-353 (1975).
13. Tomasz, A. & Beiser, S. M. *J. Bact.* **90**, 1226-1232 (1965).
14. Morrison, D. A. *J. Bact.* **136**, 548-557 (1978).
15. Morrison, D. A., Baker, M. & Mannarelli, B. in *Transformation 1978* (eds Glover, S. W. & Butler, L. O.) (Cotswood, Oxford, 1978).
16. Morrison, D. A. *J. Bact.* **132**, 576-583 (1977).
17. Laemmli, U. K. *Nature* **227**, 680-685 (1970).
18. Laskey, R. A. & Mills, A. D. *Eur. J. Biochem.* **56**, 335-341 (1975).
19. Lacks, S. J. *Bact.* **101**, 373-383 (1970).

Renal conservation of antifreeze peptide in Antarctic eelpout, *Rhigophila dearborni*

Joseph T. Eastman*, Arthur L. DeVries†, Robert E. Coalson‡, Robert E. Nordquist§ & Robert B. Boyd§

* Department of Zoology and College of Medicine, Ohio University, Athens, Ohio 45701

† Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois 61801

‡ Department of Anatomical Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73190

§ Cardiovascular-Pulmonary Division, Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104

In Antarctic notothenioid fishes large amounts (3% w/v) of small molecular weight glycoproteins lower the freezing point of the body fluids a few tenths of a degree below the freezing point of seawater (-1.9°C), enabling these animals to avoid freezing¹. Although these glycoproteins have molecular weights of 2,600-23,500 and would be expected to be filtered into the urine, they remain in the blood because the kidneys of these fishes contain only glomerular nephrons^{2,3}. Unlike the situation in most fishes, urine formation is the result of secretion rather than filtration and reabsorption. On the other hand, the peptide antifreezes in Northern Hemisphere fishes such as the winter flounder⁴, *Pseudopleuronectes americanus*, are retained by the glomerular kidney even though inulin, of comparable weight, is rapidly filtered from the blood into the urine⁵. The Antarctic eelpout (zoarcid), *Rhigophila dearborni*, which is unrelated to either the Antarctic notothenioids or *P. americanus*, also uses a peptide antifreeze (molecular weight 6,000) which is maintained at a concentration of 3% (w/v) in the blood plasma. We report here that the lack of antifreeze in the urine of *R. dearborni* probably reflects the fact that the glomeruli are not functional and cannot filter. We support this conclusion with morphological and physiological evidence and relate our findings to the conservation of biological antifreeze necessary for life in ice-laden polar waters.

Rhigophila were collected in baited traps lowered to a depth of 475-550 m through the ice at McMurdo Sound, Antarctica ($77^\circ 54' \text{S}$, $166^\circ 40' \text{E}$). The traps were retrieved 4 d later with an oceanographic winch. Fish were maintained in aquaria supplied with running water from McMurdo Sound.

Although *Rhigophila* has been reported to have glomerular kidneys³, we could not detect any peptide antifreeze in its urine on the basis of the difference between the melting point and the freezing point. We assessed glomerular filtration rate by infusing the caudal vein with the low molecular weight polysaccharide ¹⁴C-inulin which is neither secreted nor reabsorbed by the tubular epithelium. In 100 h little inulin appeared in the bladder urine. The mean ratio of ¹⁴C-inulin in urine and plasma was 0.017 (5 fish), similar to values reported for the aglomerular Antarctic cods, *Dissostichus mawsoni* and *Trematomus bernacchii*⁴. During infusion, urine flow in *Rhigophila* averaged 0.285 ml h⁻¹ kg⁻¹ of wet weight. When ³H-*p*-aminohippuric acid was infused, it appeared in the bladder urine within 1 h and maximum concentrations were observed after about 3 h when the urine/plasma ratio averaged 230. These results indicated that filtration was not involved in urine formation in *Rhigophila* even though the rate of production was similar to that of other glomerular marine teleosts.

These physiological findings led us to investigate the structure of the seemingly non-functional glomeruli of *Rhigophila*. Kidney samples were fixed for histology and electron microscopy by conventional techniques. Most Nephrons were aglomerular, and *Rhigophila* should be considered a pauciglomerular fish. The glomeruli were small compared to tubule diameter. Although some glomeruli had a few patent capillary loops, most exhibited no vascularity. Nephrons with glomeruli had short neck segments. The only other recognisable regions of the nephron were the second proximal (principal) segment and the collecting tubule, resembling the situation in truly aglomerular fishes⁶.

The squamous epithelium of the parietal layer of Bowman's capsule continued without change into the very short neck portion of the nephron. Although the lumina of Bowman's space and the neck were easily seen, it was difficult to demonstrate a direct connection between the lumina of the neck and the rest of the nephron. Serial section reconstruction verified that the epithelial components of the two portions were continuous, but continuity of the lumina could not be established. If significant amounts of glomerular filtrate were produced, the passage of filtrate into the neck would be expected to keep the lumen visible. The paucity of vascular loops within the glomerulus and the failure to demonstrate luminal patency in a portion of the nephron suggested that there was little or no filtration.

As a further test of glomerular vessel patency, Microfil (Canton Bio-Medical Products) was gravity perfused through the ventral aorta after blood had been washed out with heparinised marine teleost Ringer solution. Small arterial vessels on the capsule and in the interior of the kidney were filled, but we found no evidence of the Microfil in glomerular capillaries. We concluded that the blood supply to the kidney of *Rhigophila* was predominantly venous, as in aglomerular fishes⁶.

Ultrastructural studies confirmed that the glomeruli of *Rhigophila* were not functional. The endothelium of the glomerular capillaries was thick and lacked fenestrae (Fig. 1). The basement membranes were also thick (Fig. 1), presumably from the deposition of material produced by the mesangial cells. The cells of the visceral layer of Bowman's capsule lacked the characteristic podocyte appearance including pedicles and filtration slits (Fig. 1). These features resemble the glomerular characteristics associated with certain mammalian kidney diseases^{6,7}. We do not interpret the glomerular morphology of *Rhigophila* as pathological, but rather as a consequence of degeneration during evolution. A similar situation occurs during the regression of the larval opisthonephros in the sea lamprey, *Petromyzon marinus*⁷.

Ultrastructural features of the cells forming the principal part of the nephron included a brush border with occasional cilia, apical tubules and vesicles, numerous junctional complexes and smooth muscle cells around the tubule. There were very few lysosomes in the apical cytoplasm of the tubule cells. These organelles are normally present in tubule cells active in filtrate

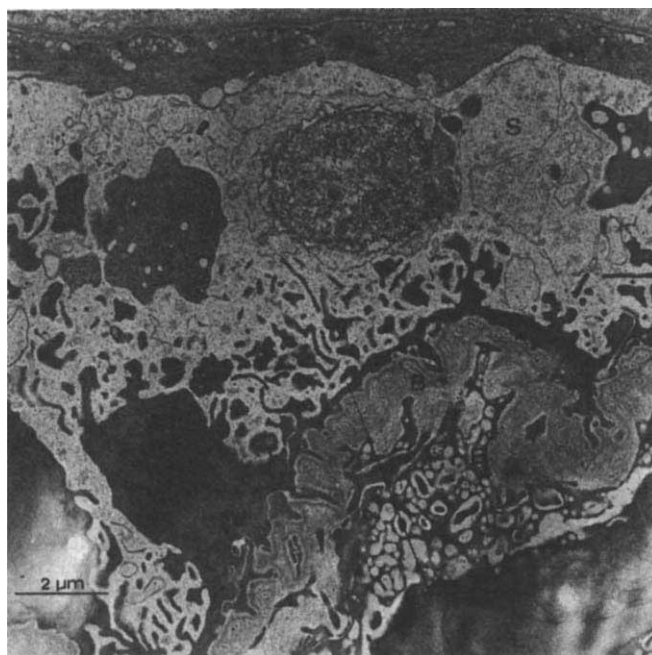


Fig. 1 Electron micrograph of a renal corpuscle from *Rhigophila*. P, parietal layer of Bowman's capsule; V, visceral layer (podocytes) of Bowman's capsule; S, Bowman's space; B, basement membrane; E, endothelium and L, lumen of glomerular capillary. The glomerular endothelium lacks fenestrations and the podocytes lack pedicles and filtration slits. Double-headed arrow indicates the thickness of the filtration barrier (about 5.0 μm).

reabsorption⁶. Their scarcity was another indication of reduced glomerular filtration in *Rhigophila*.

Rhigophila antifreeze peptide molecules are negatively charged (isoelectric point 5.5–6.0). Research on mammalian kidneys has shown that the passage of negatively charged molecules through the filtration barrier is restricted by carboxyl-rich glycoproteins in the subendothelial and subepithelial layers of the glomerular basement membrane^{8–11}. Although this mechanism may not be important in the thick glomerular walls of *Rhigophila*, it may be operational in the related north Atlantic eelpout, *Macrozoarces americanus*, and in *P. americanus*. These species filter inulin freely and also possess acidic peptides with antifreeze properties during the winter (A.L.D., unpublished data).

The reduction or loss of glomerular surface area in marine teleosts has been viewed as an energy conserving mechanism⁶. By reducing the number of small organic solutes and neutral macromolecules escaping from the plasma at the glomerulus, energy need not be expended in reabsorbing these 'useful' components from the filtrate⁶. The pauci- and aglomerular kidneys of many polar fishes have the additional advantage of preventing or minimising urinary loss of small peptides and glycoproteins with antifreeze properties². Energy conservation is likely to have been especially important in the adaptation of polar fishes to their environment, and the unusual kidneys of *Rhigophila* are an intriguing manifestation of this adaptation.

This research was supported by the US NSF.

Received 12 July; accepted 21 September 1979.

- DeVries, A. L. *Science* **172**, 1152–1155 (1971).
- Dobbs, G. H. III, Lin, Y. & DeVries, A. L. *Science* **185**, 793–794 (1974).
- Dobbs, G. H. III & DeVries, A. L. *Mar. Biol.* **29**, 59–70 (1975).
- DeVries, A. L. & Lin, Y. *Biochim. biophys. Acta* **495**, 388–392 (1977).
- Mackenzie, D. D. S., Maack, T. & Kinter, W. B. *J. exp. Zool.* **199**, 449–458 (1977).
- Hickman, C. P. Jr & Trump, B. F. in *Fish Physiology* Vol. 1 (eds Hoar, W. S. & Randall, D. J.) 91–239 (Academic, New York, 1969).
- Ooi, E. C. & Youson, J. H. *Am. J. Anat.* **154**, 57–80 (1979).
- Rennke, H. G. & Venkatachalam, M. A. *Fedn Proc.* **36**, 2619–2626 (1977).
- Caulfield, J. P. *Lab. Invest.* **40**, 503–511 (1979).
- Kanwar, Y. S. & Farquhar, M. G. *Proc. natn. Acad. Sci. U.S.A.* **76**, 1303–1307 (1979).
- Kanwar, Y. S. & Farquhar, M. G. *J. Cell Biol.* **81**, 137–153 (1979).